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#### (57) Abstract

Novel chimeric nucleic acids, encoding chimeric *Borrelia* proteins consisting of at least two antigenic polypeptides from corresponding and/or non-corresponding proteins from the same and/or different species of *Borrelia*, are disclosed. Chimeric proteins encoded by the nucleic acid sequences are also disclosed. The chimeric proteins are useful as vaccine immunogens against Lyme borreliosis, as well as for immunodiagnostic reagents.

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## CHIMERIC PROTEINS COMPRISING BORRELIA POLYPEPTIDES: USES THEREFOR

#### Background of the Invention

Lyme borreliosis is the most common tick-borne infectious disease in North America, Europe, and northern Asia. The causative bacterial agent of this disease, Borrelia burgdorferi, was first isolated and cultivated in 1982 (Burgdorferi, W.A. et al., Science 216: 1317-1319 (1982); Steere, A.R. et al., N. Engl. J. 10 Med. 308: 733-740 (1983)). With that discovery, a wide array of clinical syndromes, described in both the European and American literature since the early 20th century, could be attributed to infection by B. burgdorferi (Afzelius, A., Acta Derm. Venereol. 2: 120-15 125 (1921); Bannwarth, A., Arch. Psychiatr. Nervenkrankh. 117: 161-185 (1944); Garin, C. and A. Bujadouz, <u>J. Med. Lyon 71</u>: 765-767 (1922); Herxheimer, K. and K. Hartmann, Arch. Dermatol. Syphilol. 61: 57-76, 255-300 (1902)).

The immune response to B. burgdorferi is characterized by an early, prominent, and persistent humoral response to the end of lagellar protein, p41 (fla), and to a protein constituent of the protoplasmic cylinder, p93 (Szczepanski, A., and J.L. Benach,

Microbiol. Rev. 55:21 (1991)). The p41 flagellin antigen is an immunodominant protein; however, it shares significant homology with flagellins of other microorganisms and therefore is highly cross reactive. The p93 antigen is the largest immunodominant antigen of

30 B. burgdorferi. Both the p41 and p93 proteins are physically cryptic antigens, sheathed from the immune system by an outer membrane whose major protein constituents are the outer surface proteins A and B

(OspA and OspB). OspA is a basic lipoprotein of approximately 31 kd, which is encoded on a large linear plasmid along with OspB, a basic lipoprotein of approximately 34 kd (Szczepanski, A., and J.L. Benach, 5 Microbiol. Rev. 55:21 (1991)). Analysis of isolates of B. burgdorferi obtained from North America and Europe has demonstrated that OspA has antigenic variability, and that several distinct groups can be serologically and genotypically defined (Wilske, B., et al., World J. 10 Microbiol. 7: 130 (1991)). Other Borrelia proteins demonstrate similar antigenic variability. Surprisingly, the immune response to these outer surface proteins tends to occur late in the disease, if at all (Craft, J. E. et al., <u>J. Clin Invest. 78</u>: 934-939 15 (1986); Dattwyler, R.J. and B.J. Luft, Rheum. Clin. North Am. 15: 727-734 (1989)). Furthermore, patients acutely and chronically infected with B. burgdorferi respond variably to the different antigens, including OspA, OspB, OspC, OspD, p39, p41 and p93.

Vaccines against Lyme borreliosis have been attempted. Mice immunized with a recombinant form of OspA are protected from challenge with the same strain of B. burgdorferi from which the protein was obtained (Fikrig, E., et al., Science 250: 553-556 (1990)). 25 Furthermore, passively transferred anti-OspA monoclonal antibodies (Mabs) have been shown to be protective in mice, and vaccination with a recombinant protein induced protective immunity against subsequent infection with the homologous strain of B.burgdorferi (Simon, M.M., et 30 al., <u>J. Infect. Dis. 164</u>: 123 (1991)). Unfortunately, immunization with a protein from one strain does not necessarily confer resistance to a heterologous strain (Fikrig, E. et al., <u>J. Immunol. 7</u>: 2256-1160 (1992)), but rather, is limited to the homologous 'species' from

35 which the protein was prepared. Furthermore,

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immunization with a single protein from a particular strain of Borrelia will not confer resistance to that strain in all individuals. There is considerable variation displayed in OspA and OspB, as well as p93, including the regions conferring antigenicity. Therefore, the degree and frequency of protection from vaccination with a protein from a single strain depend upon the response of the immune system to the particular variation, as well as the frequency of genetic variation in B. burgdorferi. Currently, a need exists for a vaccine which provides immunogenicity across species and to more epitopes within a species, as well as immunogenicity against more than one protein.

#### Summary of the Invention

The current invention pertains to chimeric Borrelia 15 proteins which include two or more antigenic Borrelia polypeptides which do not occur naturally (in nature) in the same protein in Borrelia, as well as the nucleic acids encoding such chimeric proteins. The antigenic 20 polypeptides incorporated in the chimeric proteins are derived from any Borrelia protein from any strain of Borrelia, and include outer surface protein (Osp) A, OspB, OspC, OspD, p12, p39, p41, p66, and p93. The proteins from which the antigenic polypeptides are 25 derived can be from the same strain of Borrelia, from different strains, or from combinations of proteins from the same and from different strains. If the proteins from which the antigenic polypeptides are derived are OspA or OspB, the antigenic polypeptides can be derived 30 from either the portion of the OspA or OspB protein present between the amino terminus and the conserved tryptophan of the protein (referred to as a proximal portion), or the portion of the OspA or OspB protein present between the conserved tryptophan of the protein

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and the carboxy terminus (referred to as a distal portion). Particular chimeric proteins, and the nucleotide sequences encoding them, are set forth in Figures 23-37 and 43-46.

The chimeric proteins of the current invention provide antigenic polypeptides of a variety of Borrelia strains and/or proteins within a single protein. proteins are particularly useful in immunodiagostic assays to detect the presence of antibodies to native 10 Borrelia in potentially infected individuals as well as to measure T-cell reactivity, and can therefore be used as immunodiagnostic reagents. The chimeric proteins of the current invention are additionally useful as vaccine immunogens against Borrelia infection.

For a better understanding of the present invention 15 together with other and further objects, reference is made to the following description, taken together with the accompanying drawings.

#### Brief Description of the Drawings

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Figure 1 summarizes peptides and antigenic domains localized by proteolytic and chemical fragmentation of OspA.

Figure 2 is a comparison of the antigenic domains depicted in Figure 1, for OspA in nine strains of B. 25 burgdorferi.

Figure 3 is a graph depicting a plot of weighted polymorphism versus amino acid position among 14 OspA variants. The marked peaks are: a) amino acids 132-145; b) amino acids 163-177; c) amino acids 208-221. 30 lower dotted line at polymorphism value 1.395 demarcates statistically significant excesses of polymorphism at p The upper dotted line at 1.520 is the same, except that the first 29 amino acids at the monomorphic N-terminus have been removed from the original analysis.

Figure 4 depicts the amino acid alignment of residues 200 through 220 for OspAs from strains B31 and K48 as well as for the site-directed mutants 613, 625, 640, 613/625, and 613/640. Arrow indicates Trp216.

5 Amino acid changes are underlined.

Figure 5 is a helical wheel projection of residues 204-217 of B31 OspA. Capital letters indicate hydrophobic residues; lower case letters indicate hydrophilic residues; +/- indicate positively/negatively charged residues. Dashed line indicates division of the alpha-helix into hydrophobic arc (above the line) and polar arc (below the line). Adapted from France et al. (Biochem. Biophys. Acta 1120: 59 (1992)).

Figure 6 depicts a phylogenic tree for strains of

Borrelia described in Table I. The strains are as

follows: 1 = B31; 2 = Pka1; 3 = ZS7; 4 = N40; 5 =

25015; 6 = K48; 7 = DK29; 8 = PHei; 9 = Ip90; 10 =

PTrob; 11 = ACAI; 12 = PGau; 13 = Ip3; 14 = PBo; 15 =

PKo.

Figure 7 depicts the nucleic acid sequence of OspA-B31 (SEW ID NO. 6), and the encoded protein sequence (SEQ ID NO. 7).

Figure 8 depicts the nucleic acid sequence of OspA-K48 (SEQ ID NO. 8), and the encoded protein sequence 25 (SEQ ID NO. 9).

Figure 9 depicts the nucleic acid sequence of OspA-PGau (SEQ ID NO. 10), and the encoded protein sequence (SEQ ID NO. 11).

Figure 10 depicts the nucleic acid sequence of 30 OspA-25015 (SEQ ID NO. 12), and the encoded protein sequence (SEQ ID NO. 13).

Figure 11 depicts the nucleic acid sequence of OspB-B31 (SEQ ID NO. 21), and the encoded protein sequence (SEQ ID NO. 22).

Figure 12 depicts the nucleic acid sequence of OspC-B31 (SEQ ID NO. 29), and the encoded protein sequence (SEQ ID NO. 30).

Figure 13 depicts the nucleic acid sequence of 0spC-K48 (SEQ ID NO. 31), and the encoded protein sequence (SEQ ID NO. 32).

Figure 14 depicts the nucleic acid sequence of OspC-PKo (SEQ ID NO. 33), and the encoded protein sequence (SEQ ID NO. 34).

10 Figure 15 depicts the nucleic acid sequence of OspC-pTrob (SEQ ID NO. 35) and the encoded protein sequence (SEQ ID NO. 36).

Figure 16 depicts the nucleic acid sequence of p93-B31 (SEQ ID NO. 65) and the encoded protein sequence (SEQ ID NO. 66).

Figure 17 depicts the nucleic acid sequence of p93-K48 (SEQ ID NO. 67).

Figure 18 depicts the nucleic acid sequence of p93-PBo (SEQ ID NO. 69).

Figure 19 depicts the nucleic acid sequence of p93-pTrob (SEQ ID NO. 71).

Figure 20 depicts the nucleic acid sequence of p93-pGau (SEQ ID NO. 73).

Figure 21 depicts the nucleic acid sequence of p93-25 25015 (SEQ ID NO. 75).

Figure 22 depicts the nucleic acid sequence of p93-pKo (SEQ ID NO. 77).

Figure 23 depicts the nucleic acid sequence of the OspA-K48/OspA-PGau chimer (SEQ ID NO. 85) and the encoded chimeric protein sequence (SEQ ID NO. 86).

Figure 24 depicts the nucleic acid sequence of the OspA-B31/OspA-PGau chimer (SEQ ID NO. 88) and the encoded chimeric protein sequence (SEQ ID NO. 89).

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Figure 25 depicts the nucleic acid sequence of the OspA-B31/OspA-K48 chimer (SEQ ID NO. 91) and the encoded chimeric protein sequence (SEQ ID NO. 92).

Figure 26 depicts the nucleic acid sequence of the 5 OspA-B31/OspA-25015 chimer (SEQ ID NO. 94) and the encoded chimeric protein sequence (SEQ ID NO. 95).

Figure 27 depicts the nucleic acid sequence of the OspA-K48/OspA-B31/OspA-K48 chimer (SEQ ID NO. 97) and the encoded chimeric protein sequence (SEQ ID NO. 98).

Figure 28 depicts the nucleic acid sequence of the OspA-B31/OspA-K48/OspA-B31/OspA-K48 chimer (SEQ ID NO. 100) and the encoded chimeric protein sequence (SEQ ID NO. 101).

Figure 29 depicts the nucleic acid sequence of the 15 OspA-B31/OspB-B31 chimer (SEQ ID NO. 103) and the encoded chimeric protein sequence (SEQ ID NO. 104).

Figure 30 depicts the nucleic acid sequence of the OspA-B31/OspB-B31/OspC-B31 chimer (SEQ ID NO. 106) and the encoded chimeric protein sequence (SEQ ID NO. 107).

Figure 31 depicts the nucleic acid sequence of the OspC-B31/OspA-B31/OspB-B31 chimer (SEQ ID NO. 109) and the encoded chimeric protein sequence (SEQ ID NO. 110).

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Figure 32 depicts the nucleic acid sequence of the OspA-B31/p93-B31 chimer (SEQ ID NO. 111) and the encoded chimeric protein sequence (SEQ ID NO. 112).

Figure 33 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (122-234) chimer (SEQ ID NO. 113) and the encoded chimeric protein sequence (SEQ ID NO. 114).

Figure 34 depicts the nucleic acid sequence of the 30 OspB-B31/p41-B31 (122-295) chimer (SEQ ID NO. 115) and the encoded chimeric protein sequence (SEQ ID NO. 116).

Figure 35 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (140-234) chimer (SEQ ID NO. 117) and the encoded chimeric protein sequence (SEQ ID NO. 118).

Figure 36 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (140-295) chimer (SEQ ID NO. 119) and the encoded chimeric protein sequence (SEQ ID NO. 120).

Figure 37 depicts the nucleic acid sequence of the 5 OspB-B31/p41-B31 (122-234)/OspC-B31 chimer (SEQ ID NO. 121) and the encoded chimeric protein sequence (SEQ ID NO. 122).

Figure 38 depicts an alignment of the nucleic acid sequences for OspC-B31 (SEQ ID NO. 29), OspC-PKO (SEQ ID NO. 33), OspC-pTrob (SEQ ID NO. 35), and OspC-K48 (SEQ ID NO. 31). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspC-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 39 depicts an alignment of the nucleic acid sequences for OspD-pBO (SEQ ID NO. 123), OspD-pGau (SEQ ID NO. 124), OspD-DK29 (SEQ ID NO. 125), and OspD-K48 (SEQ ID NO. 126). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspD-pBo) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 40 depicts the nucleic acid sequence of p41-B31 (SEq ID NO. 127) and then encoded protein sequence (SEQ ID NO. 128).

Figure 41 depicts an alignment of the nucleic acid sequences for p41-B31 (SEQ ID NO. 127), p41-pKa1 (SEQ ID NO. 129), p41-pGau (SEQ ID NO. 51), p41-pBo (SEQ ID NO. 130), p41-DK29 (SEQ ID NO. 53), and p41-pKo (SEQ ID NO. 131). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, p41-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 42 depicts an alignment of the nucleic acid sequences for OspA-B31 (SEQ ID NO. 6), OspA-pKa1 (SEQ ID NO. 132), OspA-N40 (SEQ ID NO. 133), OspA-ZS7 (SEQ ID

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NO. 134), OspA-25015 (SEQ ID NO. 12), OspA-pTrob (SEQ ID NO. 135), OspA-K48 (SEQ ID NO. 8), OspA-Hei (SEQ ID NO. 136), OspA-DK29 (SEQ ID NO. 49), OSpA-Ip90 (SEQ ID NO. 50), OspA-pBo (Seq ID NO. 55), OspA-Ip3 (SEQ ID NO. 56), OspA-PKo (SEQ ID NO. 57), OspA-ACAI (SEQ ID NO. 58), and OspA-PGau (SEQ ID NO. 10). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspA-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 43 depicts the nucleic acid sequence of the OspA-Tro/OspA-Bo chimer (SEQ ID NO. 137) and the encoded chimeric protein sequence (SEQ ID NO. 138).

Figure 44 depicts the nucleic acid sequence of the OspA-PGau/OspA-Bo chimer (SEQ ID NO. 139) and the encoded chimeric protein sequence (SEQ ID NO. 140).

Figure 45 depicts the nucleic acid sequence of the OspA-B31/OspA-PGau/OspA-B31/OspA-K48 chimer (SEQ ID NO. 141) and the encoded chimeric protein sequence (SEQ ID NO. 142).

Figure 46 depicts the nucleic acid sequence of the OspA-PGau/OspA-B31/OspA-K48 chimer (SEQ ID NO. 143) and the encoded chimeric protein sequence (SEQ ID NO. 144).

#### Detailed Description of the Invention

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The current invention pertains to chimeric proteins
comprising antigenic Borrelia polypeptides which do not
occur in nature in the same Borrelia protein. The
chimeric proteins are a combination of two or more
antigenic polypeptides derived from Borrelia proteins.
The antigenic polypeptides can be derived from different
proteins from the same species of Borrelia, or different
proteins from different Borrelia species, as well as
from corresponding proteins from different species. As
used herein, the term "chimeric protein" describes a
protein comprising two or more polypeptides which are

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derived from corresponding and/or non-corresponding native Borrelia protein. A polypeptide "derived from" a native Borrelia protein is a polypeptide which has an amino acid sequence the same as an amino acid sequence 5 present in a Borrelia protein, an amino acid sequence equivalent to the amino acid sequence of a naturally occurring Borrelia protein, or an amino acid sequence substantially similar to the amino acid sequence of a naturally occurring Borrelia protein (e.g., differing by 10 few amino acids) such as when a nucleic acid encoding a protein is subjected to site-directed mutagenesis. "Corresponding" proteins are equivalent proteins from different species or strains of Borrelia, such as outer surface protein A (OspA) from strain B31 and OspA from 15 strain K48. The invention additionally pertains to nucleic acids encoding these chimeric proteins.

As described below, Applicants have identified two separate antigenic domains of OspA and OspB which flank the sole conserved tryptophan present in OspA and in 20 OspB. These domains share cross-reactivity with different genospecies of Borrelia. The precise amino acids responsible for antigenic variability were determined through site-directed mutagenesis, so that proteins with specific amino acid substitutions are 25 available for the development of chimeric proteins. Furthermore, Applicants have identified immunologically important hypervariable domains in OspA proteins, as described below in Example 2. The first hypervariable domain of interest for chimeric proteins, Domain A, includes amino acid residues 120-140 of OspA, the second hypervariable domain, Domain B, includes residues 150-180 and the third hypervariable domain, Domain C, includes residues 200-216 or 217 (depending on the position of the sole conserved tryptophan residue in the 35 OspA of that particular species of Borrelia) (see Figure

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3). In addition, Applicants have sequenced the genes for several Borrelia proteins.

These discoveries have aided in the development of novel recombinant Borrelia proteins which include two or more amino acid regions or sequences which do not occur in the same Borrelia protein in nature. The recombinant proteins comprise polypeptides from a variety of Borrelia proteins, including, but not limited to, OspA, OspB, OspC, OspD, p12, p39, p41, p66, and p93.

10 Antigenically relevant polypeptides from each of a number of proteins are combined into a single chimeric protein.

In one embodiment of the current invention, chimers are now available which include antigenic polypeptides 15 flanking a tryptophan residue. The antigenic polypeptides are derived from either the proximal portion from the tryptophan (the portion of the OspA or OspB protein present between the amino terminus and the conserved tryptophan of the protein), or the distal 20 portion from the tryptophan (the portion of the OspA or OspB protein present between the conserved tryptophan of the protein and the carboxy terminus) in OspA and/or The resultant chimers can be OspA-OspA chimers (i.e., chimers incorporating polypeptides derived from 25 OspA from different strains of Borrelia), OspA-OspB chimers, or OspB-OspB chimers, and are constructed such that amino acid residues amino-proximal to an invariant tryptophan are from one protein and residues carboxyproximal to the invariant tryptophan are from the other 30 protein. For example, one available chimer consists of a polypeptide derived from the amino-proximal region of OspA from strain B31, followed by the tryptophan residue, followed by a polypeptide derived from the carboxy-proximal region of OspA from strain K48 (SEQ ID 35 NO. 92). Another available chimer includes a

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polypeptide derived from the amino-proximal region of OspA from strain B31, and a polypeptide derived from the carboxy-proximal region of OspB from strain B31 (SEQ ID NO. 104). If the polypeptide proximal to the tryptophan of these chimeric proteins is derived from OspA, the proximal polypeptide can be further subdivided into the three hypervariable domains (Domains A, B, and C), each of which can be derived from OspA from a different strain of Borrelia. These chimeric proteins can further comprise antigenic polypeptides from another protein, in addition to the antigenic polypeptides flanking the tryptophan residue.

In another embodiment of the current invention, chimeric proteins are available which incorporate

15 antigenic domains of two or more *Borrelia* proteins, such as Osp proteins (Osp A, B, C and/or D) as well as pl2, p39, p41, p66, and/or p93.

The chimers described herein can be produced so that they are highly soluble, hyper-produced in E. coli, and non-lipidated. In addition, the chimeric proteins can be designed to end in an affinity tag (His-tag) to facilitate purification. The recombinant proteins described herein have been constructed to maintain high levels of antigenicity. In addition, recombinant proteins specific for the various genospecies of Borrelia that cause Lyme disease are now available, because the genes from each of the major genospecies have been sequenced; the sequences are set forth below. These recombinant proteins with their novel biophysical and antigenic properties will be important diagnostic reagent and vaccine candidates.

The chimeric proteins of the current invention are advantageous in that they retain specific reactivity to monoclonal and polyclonal antibodies against wild-type

Borrelia proteins, are immunogenic, and inhibit the

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growth or induce lysis of Borrelia in vitro.

Furthermore, in some embodiments, the proteins provide antigenic domains of two or more Borrelia strains and/or proteins within a single protein. Such proteins are particularly useful in immuno-diagostic assays. For example, proteins of the present invention can be used as reagents in assays to detect the presence of antibodies to native Borrelia in potentially infected individuals. These proteins can also be used as immunodiagnostic reagents, such as in dot blots, Western blots, enzyme linked immunosorbed assays, or agglutination assays. The chimeric proteins of the present invention can be produced by known techniques, such as by recombinant methodology, polymerase chain reaction, or mutagenesis.

Furthermore, the proteins of the current invention are useful as vaccine immunogens against Borrelia infection. Because Borrelia has been shown to be clonal, a protein comprising antigenic polypeptides from 20 a variety of Borrelia proteins and/or species, will provide immunoprotection for a considerable time when used in a vaccine. The lack of significant intragenic recombination, a process which might rapidly generate novel epitopes with changed antigenic properties, ensures that Borrelia can only change antigenic type by accumulating mutational change, which is slow when compared with recombination in generating different antigenic types. The chimeric protein can be combined with a physiologically acceptable carrier and administered to a vertebrate animal through standard methods (e.g., intravenously or intramuscularly, for example).

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The current invention is illustrated by the following Examples, which are not to be construed to be limiting in any way.

# Example 1. <u>Purification of Borrelia burgorferi Outer</u> 5 <u>Surface Protein A and Analysis of</u> Antibody Binding Domains

This example details a method for the purification of large amounts of native outer surface protein A (OspA) to homogeneity, and describes mapping of the antigenic specificities of several anti-OspA MAbs. OspA was purified to homogeneity by exploiting its resistance to trypsin digestion. Intrinsic labeling with <sup>14</sup>C-palmitic acid confirmed that OspA was lipidated, and partial digestion established lipidation at the aminoterminal cysteine of the molecule.

The reactivity of seven anti-OspA murine monoclonal antibodies to nine different Borrelia isolates was ascertained by Western blot analysis. Purified OspA was fragmented by enzymatic or chemical cleavage, and the monoclonal antibodies were able to define four distinct immunogenic domains (see Figure 1). Domain 3, which included residues 190-220 of OspA, was reactive with protective antibodies known to agglutinate the organism in vitro, and included distinct specificities, some of which were not restricted to a genotype of B. burgdorferi.

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#### Purification of Native OspA

Detergent solubilization of B. burgdorferi strips the outer surface proteins and yields partially-purified preparations containing both OspA and outer surface 5 protein B (Osp B) (Barbour, A.G. et al., Infect. Immun. 52 (5): 549-554 (1986); Coleman, J.L. and J.L. Benach, J Infect. Dis. 155 (4): 756-765 (1987); Cunningham, T.M. et al., Ann. NY Acad. Sci. 539: 376-378 (1988); Brandt, M.E. et al., <u>Infect. Immun. 58</u>: 983-991 (1990); Sambri, 10 V. and R. Cevenini, Microbiol. 14:307-314 (1991)). Although both OspA and OspB are sensitive to proteinase K digestion, in contrast to OspB, OspA is resistant to cleavage by trypsin (Dunn, J. et al., Prot. Exp. Purif. 1: 159-168 (1990); Barbour, A.G. et al., <u>Infect. Immun.</u> 15 45:94-100 (1984)). The relative insensitivity to trypsin is surprising in view of the fact that Osp A has a high (16% for B31) lysine content, and may relate to the relative configuration of Osp A and B in the outer membrane.

Intrinsic Radiolabeling of Borrelia Labeling for lipoproteins was performed as described by Brandt et al. (Infect. Immun. 58:983-991 (1990)). 14C-palmitic acid (ICN, Irvine, California) was added to the BSK II media to a final concentration of 25 0.5  $\mu$ Ci per milliliter (ml). Organisms were cultured at 34°C in this medium until a density of 108 cells per ml was achieved.

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Purification of OspA Protein from Borrelia Strain B31 Borrelia burgdorferi, either 14C-palmitic acid-30 labeled or unlabeled, were harvested and washed as described (Brandt, M.E. et al., Infect. Immun. 58:983-991 (1990)). Whole organisms were trypsinized according

to the protocol of Barbour et al. (Infect. Immun. 45:94-100 (1984)) with some modifications. The pellet was suspended in phosphate buffered saline (PBS, 10mM, pH 7.2), containing 0.8% tosyl-L-phenylalanine chloromethyl 5 ketone (TPCK)-treated trypsin (Sigma, St. Louis, Missouri), the latter at a ratio of 1  $\mu$ g per 10 $^{8}$  cells. Reaction was carried out at 25°C for 1 hour, following which the cells were centrifuged. The pellet was washed in PBS with 100  $\mu g/ml$  phenylmethylsulfonyl fluoride 10 (PMSF). Triton X-114 partitioning of the pellet was carried out as described by Brandt et al. (Infect. Immun. 58:983-991 (1990)). Following trypsin treatment, cells were resuspended in ice-cold 2% (V/V) Triton X-114 in PBS at 10° cells per ml. The suspension was rotated 15 overnight at 4°C, and the insoluble fraction removed as a pellet after centrifugation at 10,000 X g for 15 minutes at 4°C. The supernatant (soluble fraction) was incubated at 37°C for 15 minutes and centrifuged at room temperature at 1000 X g for 15 minutes to separate the 20 aqueous and detergent phases. The aqueous phase was decanted, and ice cold PBS added to the lower Triton phase, mixed, warmed to 37°C, and again centrifuged at 1000 X g for 15 minutes. Washing was repeated twice more. Finally, detergent was removed from the 25 preparation using a spin column of Bio-beads SM2 (BioRad, Melville, New York) as described (Holloway, P.W., Anal. Biochem. 53:304-308 (1973)).

Ion exchange chromatography was carried out as described by Dunn et al. (Prot. Exp. Purif. 1: 159-168 (1990)) with minor modifications. Crude OspA was dissolved in buffer A (1% Triton X-100, 10mM phosphate buffer (pH 5.0)) and loaded onto a SP Sepharose resin (Pharmacia, Piscataway, New Jersey), pre-equilibrated with buffer A at 25°C. After washing the column with 10

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bed-volumes of buffer A, the bound OspA was eluted with buffer B (1% Triton X-100, 10mM phosphate buffer (pH 8.0)). OspA fractions were detected by protein assay using the BCA method (Pierce, Rockford, Illinois), or as radioactivity when intrinsically labeled material was fractionated. Triton X-100 was removed using a spin column of Bio-beads SM2.

This method purifies OspA from an outer surface membrane preparation. In the absence of trypsin
10 treatment, OspA and B were the major components of the soluble fraction obtained after Triton partitioning of strain B31. In contrast, when Triton extraction was carried out after trypsin-treatment, the OspB band is not seen. Further purification of OspA-B31 on a SP

15 Sepharose column resulted in a single band by SDS-PAGE. The yield following removal of detergent was approximately 2 mg per liter of culture. This method of purification of OspA, as described herein for strain B31, can be used for other isolates of Borrelia as well.

20 For strains such as strain K48, which lack OspB, trypsin treatment can be omitted.

#### Lipidation site of OspA-B31

14C-palmitic acid labeled OspA from strain B31 was purified as described above and partially digested with endoproteinase Asp-N (data not shown). Following digestion, a new band of lower molecular weight was apparent by SDS-PAGE, found by direct amino-terminal sequencing to begin at Asp<sub>25</sub>. This band had no trace of radioactivity by autoradiography (data not shown). OspA and B contain a signal sequence (L-X-Y-C) similar to the consensus described for lipoproteins of E. coli, and it has been predicted that the lipidation site of OspA and B should be the amino-terminal cysteine (Brandt, M.E. et

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al., <u>Infect. Immun 58</u>: 983-991 (1990)). The results presented herein support this prediction.

### B. Comparison of OspA Antibody Binding Regions in Nine Strains of Borrelia burgdorferi

The availability of the amino acid sequenced for OspA from a number of different isolates, combined with peptide mapping and Western blot analysis, permitted the identification of the antigenic domains recognized by monoclonal antibodies (MAbs) and allowed inference of the key amino acid residues responsible for specific antibody reactivity.

Strains of Borrelia burgdorferi

Nine strains of *Borrelia*, including seven European strains and two North American strains, were used in this study of antibody binding domains of several proteins. Information concerning the strains is summarized in Table I, below.

Table I. Representative Borrelia Strains

Table 1. Representative Boiletta Strains				
Strain	Location and Source	Reference for Strain		
K48	Czechoslovakia, Ixodes ricinus	none		
PGau	Germany, human ACA	Wilske, B. et al., <u>J. Clin.</u> <u>Microbiol. 32</u> :340-350 (1993)		
DK29	Denmark, human EM	Wilske, B. et al.		
PKo	Germany, human EM	Wilske, B. et al.		
PTrob	Germany, human skin	Wilske, B. et al.		
Ip3	Khabarovsk, Russia, I. persulcatus	Asbrink, E. et al., <u>Acta</u> <u>Derm. Venereol. 64</u> : 506-512 (1984)		
Ip90	Khabarovsk, Russia, I. persulcatus	Asbrink, E. et al.		
25015	Millbrook, NY, I. persulcatus	Barbour, A.G. et al., <u>Curr.</u> <u>Microbiol.</u> 8:123-126 (1983)		
B31	Shelter Island, NY, I. scapularis	Luft, B.J. et al., <u>Infect.</u> <u>Immun. 60</u> : 4309-4321 (1992); ATCC 35210		
PKa1	Germany, human CSF	Wilske, B. et al.		
ZS7	Freiburg, Germany, I. ricinus	Wallich, R. et al., <u>Nucl.</u> <u>Acids Res. 17</u> : 8864 (1989)		
N40	Westchester Co., NY	Fikrig, E. et al., <u>Science</u> 250:553-556 (1990)		
PHei	Germany, human CSF	Wilske, B. et al.		
ACAI	Sweden, human ACA	Luft, B. J. et al., <u>FEMS</u> <u>Microbiol. Lett. 93</u> :73-68 (1992)		
PBo	Germany, human CSF	Wilske, B. et al.		

ACA = patient with acrodermatitis chronica atrophicans; EM = patient with erythema migrans; CSF = cerebrospinal fluid of patient with Lyme disease

Strains K48, PGau and DK29 were supplied by R. Johnson, University of Minnesota; PKo and pTrob were provided by B. Wilske and V. Preac-Mursic of the

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Pettenkhofer Institute, Munich, Germany; and Ip3 and Ip90 were supplied by L. Mayer of the Center for Disease Control, Atlanta, Georgia. The North American strains included strain 25015, provided by J. Anderson of the Connecticut Department of Agriculture; and strain B31 (ATCC 35210).

#### Monoclonal Antibodies

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Seven monoclonal antibodies (MAbs) were utilized in this study. Five of the MAbs (12, 13, 15, 83 and 336) were 10 produced from hybridomas cloned and subcloned as previously described (Schubach, W.H., et al., Infect. Immun. 59(6):1911-1915 (1991)). MAb H5332 (Barbour, A.G. et al., Infect. Immun. 41:795-804 (1983)) was a gift from Drs. Alan Barbour, University of Texas, and MAb CIII.78 (Sears, J.E. 15 et al., <u>J. Immunol. 147</u>(6):1995-2000 (1991)) was a gift from Richard A. Flavell, Yale University. MAbs 12 and 15 were raised against whole sonicated B3; MAb 336 was produced against whole PGau; and MAbs 13 and 83 were raised to a truncated form of OspA cloned from the K48 strain and 20 expressed in E. coli using the T7 RNA polymerase system (McGrath, B.C. et al., Vaccines, Cold Spring Harbor Laboratory Press, Plainview, New York, pp. 365-370 (1993)). All MAbs were typed as being Immunoglobulin G (IgG).

Methods of Protein Cleavage, Western Blotting, and Amino-Terminal Sequencing

Prediction of the various cleavage sites was achieved by knowledge of the primary amino acid sequence derived from the full nucleotide sequences of OspA, many of which are currently available (see Table II, below). Cleavage sites can also be predicted based on the peptide sequence of OspA, which can be determined by standard techniques after isolation and purification of OspA by the method described above. Cleavage of several OspA isolates was

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conducted to determine the localization of monoclonal antibody binding of the proteins.

Hydroxylamine-HCl (HA), N-chlorosuccinimide (NCS), and cyanogen bromide cleavage of OspA followed the methods

5 described by Bornstein (Biochem. 9 (12):2408-2421 (1970)), Shechter et al., (Biochem. 15 (23):5071-5075 (1976)), and Gross (in Hirs, C.H.W. (ed): Methods in Enzymology, (N.Y. Acad. Press), 11:238-255 (1967)) respectively. Protease cleavage by endoproteinase, Asp-N (Boehringer Mannheim,

10 Indianapolis, Indiana), was performed as described by Cleveland D.W. et al., (J. Biol. Chem. 252:1102-1106 (1977)). Ten micrograms of OspA were used for each reaction. The ratio of enzyme to OspA was approximately 1 to 10 (w/w).

Proteins and peptides generated by cleavage were separated by SDS-polyacrylamide gel electrophoresis (SDS-PAGE) (Laemmli, U.K., Nature (London) 227:680-685 (1970)), and electroblotted onto immobilon Polyvinylidine Difluoride (PVDF) membranes (Ploskal, M.G. et al., Biotechniques

20 4:272-283 (1986)). They were detected by amido black staining or by immunostaining with murine MAbs, followed by alkaline phosphatase-conjugated goat antimouse IgG. Specific binding was detected using a 5-bromo-4-chloro-3-indolylphosphate (BCIP)/nitroblue tetrazolium (NBT)

25 developer system (KPL Inc., Gathersburg, Maryland).

In addition, amino-terminal amino acid sequence analysis was carried out on several cleavage products, as described by Luft et al. (Infect. Immun. 57:3637-3645 (1989)). Amido black stained bands were excised from PVDF blots and sequenced by Edman degradation using a Biosystems model 475A sequenator with model 120A PTH analyzer and model 900A control/data analyzer.

Cleavage Products of Outer Surface Protein A Isolates Purified OspA-B31, labeled with 14C-palmitic acid, was fragmented with hydroxylamine-HCl (HA) into two peptides, designated HA1 and HA2 (data not shown). The HA1 band 5 migrated at 27 KD and retained its radioactivity, indicating that the peptide included the lipidation site at the N-terminus of the molecule (data not shown). From the predicted cleavage point, HA1 should correspond to residues 1 to 251 of OspA-B31. HA2 had a MW of 21.6 KD by SDS-PAGE, 10 with amino-terminal sequence analysis showing it to begin at Gly72, i.e. residues 72 to 273 of OspA-B31. By contrast, HA cleaved OspA-K48 into three peptides, designated HA1, HA2, and HA3 with apparent MWs of 22KD, 16 KD and 12 KD, respectively. Amino-terminal sequencing 15 showed HA1 to start at Gly72, and HA3 at Gly142. HA2 was found to have a blocked amino-terminus, as was observed for the full-length OspA protein. HA1, 2 and 3 of OspA-K48 were predicted to be residues 72-274, 1 to 141 and 142 to 274, respectively.

N-Chlorosuccinimide (NCS) cleaves tryptophan (W), which is at residue 216 of OspA-B31 or residue 217 of OspA-K48 (data not shown). NCS cleaved OspA-B31 into 2 fragments, NCS1, with MW of 23 KD, residues 1-216 of the protein, and NCS2 with a MW of 6.2 KD, residues 217 to 273 (data not shown). Similarly, K48 OspA was divided into 2 pieces, NCS1 residues 1-217, and NCS2 residues 218 to 274 (data not shown).

Cleavage of OspA by cyanogen bromide (CNBr) occurs at the carboxy side of methionine, residue 39. The major fragment, CNBr1, has a MW of 25.7 KD, residues 39-274 by amino-terminal amino acid sequence analysis (data not shown). CNBr2 (about 4 KD) could not be visualized by amido black staining; instead, lightly stained bands of about 20 KD MW were seen. These bands reacted with anti-

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OspA MAbs, and most likely were degradation products due to cleavage by formic acid.

Determination of Antibody Binding Domains for Anti-OspA Monoclonal Antibodies

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The cleavage products of OspA-B31 and OspA-K48 were analyzed by Western blot to assess their ability to bind to the six different MAbs. Preliminary Western blot analysis of the cleavage products demonstrated that strains K48 and DK29 have similar patterns of reactivity, as do IP3, PGau 10 and PKo. The OspA of strain PTrob was immunologically distinct from the others, being recognized only by MAb 336. MAb 12 recognized only the two North American strains, B31 and 25015. When the isolates were separated into genogroups, it was remarkable that all the MAbs, except MAb 15 12, crossed over to react with multiple genogroups.

MAb12, specific for OspA-B31, bound to both HA1 and HA2 of OspA-B31. However, cleavage of OspA-B31 by NCS at residue Trp216 created fragments which did not react with MAb12, suggesting that the relevant domain is near or is 20 structurally dependent upon the integrity of this residue (data not shown). MAb 13 bound only to OspA-K48, and to peptides containing the amino-terminus of that molecule (e.g. HA2; NCS1). It did not bind to CNBr1 residues 39 to Thus the domain recognized by MAb13 is in the amino-25 terminal end of OspA-K48, near Met38.

MAb15 reacts with the OspA of both the B31 and K48 strains, and to peptides containing the N-terminus of OspA, such as HA1 of OspA-B31 and NCS1, but not to peptides HA2 of OspA-B31 and HA1 of OspA-K48 (data not shown). Both 30 peptides include residue 72 to the C-terminus of the molecules. MAb15 bound to CNBr1 of OspA-K48, indicating the domain for this antibody to be residues 39 to 72, specifically near Gly72 (data not shown).

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MAD83 binds to OspA-K48, and to peptides containing the C-terminal portion of the molecule, such as HA1. They do not bind to HA2 of OspA-K48, most likely because the C-terminus of HA2 of OspA-K48 ends at 141. Similar to MAD12 and OspA-B31, binding of MADs 83 and CIII.78 is eliminated by cleavage of OspA at the tryptophan residue. Thus binding of MADs 12, 83 and CIII.78 to OspA depends on the structural integrity of the Trp216 residue, which appears to be critical for antigenicity. Also apparent is that, although these MADs bind to a common antigenic domain, the precise epitopes which they recognize are distinct from one another given the varying degrees of cross-reactivity to these MADs among strains.

Although there is similar loss of binding activity of

MAb336 with cleavage at Trp216, this MAb does not bind to

HA1 of OspA-B31, suggesting the domain for this antibody

includes the carboxy-terminal end of the molecule,

inclusive of residues 251 to 273. Low MW peptides, such as

HA3 (10 KD) and NCS2 (6KD), of OspA-K48 do not bind this

MAb on Western blots. In order to confirm this

observation, we tested binding of the 6 MAbs with a

recombinant fusion construct p3A/EC that contains a trpE

leader protein fused with residues 217 to 273 of OspA-B31

(Schubach, W.H. et al., Infect. Immun. 59(6): 1911-1915

(1991)). Only MAb336 reacted with this construct (data not shown). Peptides and antigenic domains localized by

fragmentation of OspA are summarized in Figure 1.

Mapping of Domains to Define the Molecular Basis for the Serotype Analysis

To define the molecular basis for the serotype analysis of OspA, we compared the derived amino acid sequences of OspA for the nine isolates (Figure 2). At the amino terminus of the protein, these predictions can be more precise given the relatively small number of amino

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acid substitutions in this region compared to the carboxy terminus. Domain 1, which is recognized by MAb13, includes residues Leu34 to Leu41. MAb13 only binds to the OspA of species K48, DK29 and IP90. Within this region, residue 37 5 is variable, however Gly37 is conserved amongst the three reactive strains. When Gly37 is changed to Glu37, as it is in OspA of strains B31, pTrob, PGau, and PKo, MAb13 does not recognize the protein (data not shown). By similar analysis, it can be seen that Asp70 is a crucial residue 10 for Domain 2, which includes residues 65 to 75 and is recognized by MAb15. Domain 3 is reactive with MAbs H5332, 12 and 83, and includes residues 190-220. It is clear that significant heterogeneity exists between MAbs reactive with this domain, and that more than one conformational epitope 15 must be contained within the sequence. Domain 4 binds MAb336, and includes residues 250 to 270. In this region, residue 266 is variable and therefore may be an important determinant. It is apparent, however, that other determinants of the reactivity of this monoclonal antibody 20 reside in the region comprising amino acids 217-250. Furthermore, the structural integrity of Trp216 is essential for antibody reactivity in the intact protein. Finally, it is important to stress that Figure 2 indicates only the locations of the domains, and does not necessarily 25 encompass the entire domain. Exact epitopes are being analyzed by site-directed mutagenesis of specific residues.

Overall, evidence suggests that the N-terminal portion is not the immunodominant domain of OspA, possibly by virtue of its lipidation, and the putative function of the lipid moiety in anchoring the protein to the outer envelope. The C-terminal end is immunodominant and includes domains that account in part for structural heterogeneity (Wilske, B. et al., Med. Microbiol. Immunol. 181: 191-207 (1992)), and may provide epitopes for antibody

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neutralization (Sears, J.E. et al., J. Immunol. 147(6):
1995-2000 (1991)), and relate to other activities, such as
the induction of T-cell proliferation (Shanafel, M.M., et
al., J. Immunol. 148: 218-224 (1992)). There are common
epitopes in the carboxy-end of the protein that are shared
among genospecies which may have immunoprotective potential
(Wilske, B., et al., Med. Microbiol. Immunol. 181: 191-207
(1992)).

Prediction of secondary structure on the basis of

hydropathy analysis and circular dichroism and fluorescence spectroscopy measurements (McGrath, B.C., et al., Vaccines, Cold Spring Harbor Laboratory Press, Plainview, New York; pp. 365-370 (1993)) suggest domains 3 and 4 to be in a region of the molecule with a propensity to form alphabelix, whereas domains 1 and 2 occur in regions predicted to be beta-sheets (see Figure 1). These differences may distinguish domains in accessibility to antibody or to reactive T-cells (Shanafel, M.M. et al., J. Immunol. 148: 218-224 (1992)). Site-directed mutagenesis of specific epitopes, as described below in Example 2, aids in identifying exact epitopes.

# Example 2. Identification of an Immunologically Important Hypervariable Domain of the Major Outer Surface Protein A of Borrelia

This Example describes epitope mapping studies using chemically cleaved OspA and TrpE-OspA fusion proteins. The studies indicate a hypervariable region surrounding the single conserved tryptophan residue of OspA (at residue 216, or in some cases 217), as determined by a moving window population analysis of OspA from fifteen European and North American isolates of Borrelia. The hypervariable region is important for immune recognition.

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Site-directed mutagenesis was also conducted to examine the hypervariable regions more closely. Fluorescence and circular dichroism spectroscopy have indicated that the conserved tryptophan is part of an 5 alpha-helical region in which the tryptophan is buried in a hydrophobic environment (McGrath, B.C., et al., Vaccines, Cold Spring Harbor Laboratory Press, Plainview, New York; pp. 365-370 (1993)). More polar amino acid side-chains flanking the tryptophan are likely to be exposed to the 10 hydrophilic solvent. The hypervariability of these solvent-exposed residues among the various strains of Borrelia suggested that these amino acid residues may contribute to the antigenic variation in OspA. Therefore, site-directed mutagenesis was performed to replace some of 15 the potentially exposed amino acid side chains in the protein from one strain with the analogous residues of a second strain. The altered proteins were then analyzed by Western Blot using monoclonal antibodies which bind OspA on the surface of the intact, non-mutated spirochete. 20 results indicated that certain specific amino acid changes near the tryptophan can abolish reactivity of OspA to these monoclonal antibodies.

#### Verification of Clustered Polymorphisms in Outer <u>A.</u> Surface Protein A Sequences

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Cloning and sequencing of the OspA protein from fifteen European and North American isolates (described above in Table I) demonstrated that amino acid polymorphism is not randomly distributed throughout the protein; rather, polymorphism tended to be clustered in three regions of 30 OspA. The analysis was carried out by plotting the moving, weighted average polymorphism of a window (a fixed length subsection of the total sequence) as it is slid along the sequence. The window size in this analysis was thirteen amino acids, based upon the determination of the largest

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number of significantly deviating points as established by the method of Tajima (<u>J. Mol. Evol. 33</u>: 470-473 (1991)). The average weighted polymorphism was calculated by summing the number of variant alleles for each site. Polymorphism 5 calculations were weighted by the severity of amino acid replacement (Dayhoff, M.O. et al., in: Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure NBRF, Washington, Vol. 5, Suppl. 3: 345 (1978)). The sum was normalized by the window size and plotted. The amino acid sequence 10 position corresponds to a window that encompasses amino acids 1 through 13. Bootstrap resampling was used to generate 95% confidence intervals on the sliding window analysis. Since Borrelia has been shown to be clonal, the bootstrap analysis should give a reliable estimate of the 15 expected variance out of polymorphism calculations. bootstrap was iterated five hundred times at each position, and the mean was calculated from the sum of all positions. The clonal nature of Borrelia ensures that the stochastic variance that results from differing genealogical histories 20 of the sequence positions (as would be expected if recombination were prevalent) will be minimized.

This test verified that the three regions around the observed peaks all have significant excesses of polymorphism. Excesses of polymorphism were observed in the regions including amino acid residues 132-145, residues 163-177, and residues 208-221 (Figure 3). An amino acid alignment between residues 200 and 220 for B31, K48 and the four site-directed mutants is shown in Figure 4. The amino acid 208-221 region includes the region of OspA which has been modeled as an oriented alpha-helix in which the single tryptophan residue at amino acid 216 is buried in a hydrophobic pocket, thereby exposing more polar amino acids to the solvent (Figure 5) (France, L.L., et al., Biochem. Biophys. Acta 1120: 59 (1992)). These potentially solvent-exposed residues showed considerable variability among the

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OspAs from various strains and may be an important component of OspA antigenic variation. For the purposes of generating chimeric proteins, the hypervariable domains of interest are <u>Domain A</u>, which includes amino acid residues 120-140 of OspA; <u>Domain B</u>, which includes residues 150-180; and <u>Domain C</u>, which includes residues 200-216 or 217.

- B. Site-Directed Mutagenesis of the Hypervariable Region
  Site-directed mutagenesis was performed to convert
  residues within the 204-219 domain of the recombinant B31

  10 OspA to the analogous residues of a European OspA variant,
  K48. In the region of OspA between residues 204 and 219,
  which includes the helical domain (amino acids 204-217),
  there are seven amino acid differences between OspA-B31 and
  OspA-K48. Three oligonucleotides were generated, each
  15 containing nucleotide changes which would incorporate K48
  amino acids at their analogous positions in the B31 OspA
  protein. The oligos used to create the site-directed
  mutants were:
- 5'-CTTAATGACTCTGACACTAGTGC-3' (#613, which converts

  threonine at position 204 to serine, and serine at 206 to
  threonine (Thr204-Ser, Thr206-Ser)) (SEQ ID NO. 1);

  5'-GCTACTAAAAAAACCGGGAAATGGAATTCA-3' (#625, which converts
  alanine at 214 to glycine, and alanine at 215 to lysine
  (Ala214-Gly, Ala215-Lys)) (SEQ ID NO. 2); and
  - 5'-GCAGCTTGGGATTCAAAAACATCCACTTTAACA-3' (#640, which converts asparagine at 217 to aspartate, and glycine at 219 to lysine (Asn217-Asp, Gly219-Lys)) (SEQ ID NO. 3).

25

Site-directed mutagenesis was carried out by performing mutagenesis with pairs of the above oligos.

Three site-directed mutants were created, each with two changes: OspA 613 (Thr204-Ser, Thr206-Ser), OspA 625 (Ala214-Gly, Ala215-Lys), and 640 (Asn217-Asp, Gly219-Lys). There were also two proteins with four changes: OspA 613/625 (Thr204-Ser, Thr206-Ser, Ala214-Gly, Ala215-Lys)

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and OspA 613/640 (Thr204-Ser, Thr206-Ser, Asn217-Asp, Gly219-Lys).

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Specificity of Antibody Binding to Epitopes of the Non-mutated Hypervariable Region

Monoclonal antibodies that agglutinate spirochetes, including several which are neutralizing in vitro, recognize epitopes that map to the hypervariable region around Trp216 (Barbour, A.G. et al., Infect. and Immun. 41: 759 (1983); Schubach, W.H. et al., Infect. and Immun. 59:

10 1911 (1991)). Western Blot analysis demonstrated that chemical cleavage of OspA from the B31 strain at Trp 216 abolishes reactivity of the protein with the agglutinating Mab 105, a monoclonal raised against B31 spirochetes (data not shown). The reagent, n-chlorosuccinimide (NCS),

15 cleaves OspA at the Trp 216, forming a 23.2kd fragment and a 6.2kd peptide which is not retained on the Imobilon-P membrane after transfer. The uncleaved material binds Mab 105; however, the 23.2kd fragment is unreactive. Similar Western blots with a TrpE-OspA fusion protein containing

the carboxy-terminal portion of the OspA protein demonstrated that the small 6.2kd piece also fails to bind Mab 105 (Schubach, W.H. et al., <u>Infect. and Immun. 59</u>: 1911 (1991)).

Monoclonal antibodies H5332 and H3TS (Barbour, A.G. et al., Infect. and Immun. 41: 759 (1983)) have been shown by immunofluorescence to decorate the surface of fixed spirochetes (Wilske, B. et al., World J. Microbiol. 7: 130 (1991)). These monoclonals also inhibit the growth of the organism in culture. Epitope mapping with fusion proteins has confirmed that the epitopes which bind these Mabs are conformationally determined and reside in the carboxy half of the protein. Mab H5332 is cross-reactive among all of the known phylogenetic groups, whereas Mab H3TS and Mab 105 seem to be specific to the B31 strain to which they were

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raised. Like Mab 105, the reactivities of H5332 and H3TS to OspA are abrogated by fragmentation of the protein at Trp216 (data not shown). Mab 336 was raised to whole spirochetes of the strain P/Gau. It cross-reacts to OspA from group 1 (the group to which B31 belongs) but not to group 2 (of which K48 is a member). Previous studies using fusion proteins and chemical cleavage have indicated that this antibody recognizes a domain of OspA in the region between residues 217 and 273 (data not shown). All of these Mabs will agglutinate the B31 spirochete.

Western Blot Analysis of Antibody Binding to Mutated Hypervariable Regions

Mabs were used for Western Blot analysis of the sitedirected OspA mutants induced in E.coli using the T7

15 expression system (Dunn, J.J. et al., Protein Expression
and Purification 1: 159 (1990)). E. coli cells carrying
Pet9c plasmids having a site-directed OspA mutant insert
were induced at mid-log phase growth with IPTG for four
hours at 37°C. Cell lysates were made by boiling an
20 aliquot of the induced cultures in SDS gell loading dye,
and this material was then loaded onto a 12% SDS gell
(BioRad mini-Protean II), and electrophoresed. The
proteins were then transferred to Imobilon-P membranes
(Millipore) 70V, 2 hour at 4°C using the BioRad mini
25 transfer system. Western analysis was carried out as
described by Schubach et al. (Infect. Immun. 59: 1911
(1991)).

Western Blot analysis indicated that only the 625 mutant (Ala214-Gly and Ala215-Lys) retained binding to the agglutinating monoclonal H3TS (data not shown). However, the 613/625 mutant which has additional alterations to the amino terminus of Trp216 (Ser204-Thr and Thr206-Ser) did not bind this monoclonal. Both 640 and 613/640 OspAs which have the Asn217-Asp and Gly219-Lys changes on the carboxy-

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terminal side of Trp216 also failed to bind Mab H3TS. indicated that the epitope of the B31 OspA which binds H3TS is comprised of amino acid side-chains on both sides of Trp216.

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The 613/625 mutant failed to bind Mabs 105 and H5332, while the other mutants retained their ability to bind these Mabs. This is important in light of the data using fusion proteins that indicate that Mab 105 behaves more like Mab H3TS in terms of its serotype specificity and 10 binding to OspA (Wilske, B. et al., Med. Microbiol. Immunol. 181: 191 (1992)). The 613/625 protein has, in addition to the differences at residues Thr204 and Ser206, changes immediately amino-terminal to Trp216 (Ala214-Gly and Ala215-Lys). The abrogation of reactivity of Mabs 105 and H5332 to this protein indicated that the epitopes of OspA which bind these monoclonals are comprised of residues on the amino-terminal side of Trp216.

The two proteins carrying the Asn217-Asp and Gly219-Lys replacements on the carboxy-terminal side of Trp216 20 (OspAs 640 and 613/640) retained binding to Mabs 105 and H5332; however, they failed to react with Mab 336, a monoclonal which has been mapped with TrpE-OspA fusion proteins and by chemical cleavage to a more carboxyterminal domain. This result may explain why Mab 336 25 failed to recognize the K48-type of OspA (Group 2).

It is clear that amino acids Ser204 and Thr206 play an important part in the agglutinating epitopes in the region of the B31 OspA flanking Trp216. Replacement of these two residues altered the epitopes of OspA that bind Mabs 105, 30 H3TS and H5332. The ability of the 640 changes alone to abolish reactivity of Mab 336 indicated that Thr204 and Ser206 are not involved in direct interaction with Mab 336.

The results indicated that the epitopes of OspA which are available to Mabs that agglutinate spirochetes are 35 comprised at least in part by amino acids in the immediate

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vicinity of Trp216. Since recent circular dichroism analysis indicated that the structures of B31 and K48 OspA differ very little within this domain, it is unlikely that the changes made by mutation have radically altered the overall structure of the OspA protein (France, L.L. et al., Biochem. Biophys. Acta 1120: 59 (1992); and France et al., Biochem. Biophys Acta, submitted (1993)). This hypothesis is supported by the finding that the recombinant, mutant OspAs exhibit the same high solubility and purification properties as the parent B31 protein (data not shown).

In summary, amino acid side-chains at Ser204 and Thr206 are important for many of the agglutinating epitopes. However, a limited set of conservative changes at these sites were not sufficient to abolish binding of all of the agglutinating Mabs. These results suggested that the agglutinating epitopes of OspA are distinct, yet may have some overlap. The results also supported the hypothesis that the surface-exposed epitope around Trp216 which is thought to be important for immune recognition and neutralization is a conformationally-determined and complex domain of OspA.

#### EXAMPLE 3. Borrelia Strains and Proteins

Proteins and genes from any strain of Borrelia can be utilized in the current invention. Representative strains are summarized in Table I, above.

#### A. Genes Encoding Borrelia Proteins

The chimeric peptides of the current invention can comprise peptides derived from any Borrelia proteins.

Representative proteins include OspA, OspB, OspC, OspD,

p12, p39, p41 (fla), p66, and p93. Nucleic acid sequences encoding several Borrelia proteins are presently available (see Table II, below); alternatively, nucleic acid

sequences encoding Borrelia proteins can be isolated and characterized using methods such as those described below.

Table II. References for Nucleic Acid Sequences for Several Proteins of Various Borrelia Strains

Strai n	p93	OspA	p41 (fla)			
K48	X69602 (SID 67)	X62624 (SID 8)	X69610 (SID 49)			
PGau	SID 73	X62387 (SID 10)	X69612 (SID 51)			
DK29	-	X63412 (SID 137)	X69608 (SID 53)			
PKo	X69803 (SID 77)	X65599 (SID 141)	X69613 (SID 131)			
PTrob	X69604 (SID 71)	X65598 (SID 135)	X69614 (SID 55)			
Ip3	-	X70365 (SID 140)	-			
Ip90	ND	Kryuchechnikov, V.N. et al., <u>J.Microbiol.</u> <u>Epid. Immunobiol.</u> <u>12</u> :41-44 (1988) (SID 138)	-			
25015	X70365 (SID 75)	Fikrig, E.S. et al., <u>J. Immunol. 7</u> :2256- 2260 1992) SID 12)	-			
B31	Perng, G.C. et al., <u>Infect.</u> <u>Immun. 59:</u> 2070- 74 (1992); Luft, B.J. et al., <u>Infect.</u> <u>Immun. 60:</u> 4309- 4321 (1992) (SID 65)	Bergstrom, S. et al., Mol. Microbiol. 3:479-486 (1989) (SID 6)	Gassmann, G.S. et al., <u>Nucl.</u> <u>Acids Res. 17</u> : 3590 (1989) (SID 127)			
PKa1		X69606 (SID 132)	X69611 (SID 129)			
ZS7	-	Jonsson, M. et al., <u>Infect. Immun.</u> <u>60</u> :1845-1853 (1992) (SID 134)	-			
N40	-	Kryuchechnikov, V.N. et al. (SID 133)	-			
PHei	-	X65600 (SID 136)	-			
ACAI	-	Kryuchechnikov, V.N. et al. (SID 142)	-			
РВо	X69601 (SID 69)	X65605 (SID 139)	X69610 (SID 130)			

Numbers with an "X" prefix are GenBank data base accession numbers. SID = SEQ ID NO.

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## B. <u>Isolation of Borrelia Genes</u>

Nucleic acid sequences encoding full length, lipidated proteins from known Borrelia strains were isolated using the polymerase chain reaction (PCR) as described below. In 5 addition, nucleic acid sequences were generated which encoded truncated proteins (proteins in which the lipidation signal has been removed, such as by eliminating the nucleic acid sequence encoding the first 18 amino acids, resulting in non-lipidated proteins). Other 10 proteins were generated which encoded polypeptides of a particular gene (i.e., encoding a segment of the protein which has a different number of amino acids than the protein does in nature). Using similar methods as those described below, primers can be generated from known 15 nucleic acid sequences encoding Borrelia proteins and used to isolate other genes encoding Borrelia proteins. Primers can be designed to amplify all of a gene, as well as to amplify a nucleic acid sequence encoding truncated protein sequences, such as described below for OspC, or nucleic 20 acid sequences encoding a polypeptide derived from a Borrelia protein. Primers can also be designed to incorporate unique restriction enzyme cleavage sites into the amplified nucleic acid sequences. Sequence analysis of the amplified nucleic acid sequences can then be performed 25 using standard techniques.

> Cloning and Sequencing of OspA Genes and Relevant Nucleic Acid Sequences

Borrelia OspA sequences were isolated in the following manner: 100 μl reaction mixtures containing 50 mM KCl, 10 mM TRIS-HCl (pH 8,3), 1.5 mM MgCl<sub>2</sub>, 200 μM each NTP, 2.5 units of TaqI DNA polymerase (Amplitaq, Perkin-Elmer/Cetus) and 100 pmol each of the 5' and 3' primers (described below) were used. Amplification was performed in a Perkin-Elmer/Cetus thermal cycler as described (Schubach, W.H. et

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al., Infect. Immun. 59:1811-1915 (1991)). The amplicon was
visualized on an agarose gel by ethidium bromide staining.
Twenty nanograms of the chloroform-extracted PCR product
were cloned directly into the PC-TA vector (Invitrogen) by
following the manufacturer's instructions. Recombinant
colonies containing the amplified fragment were selected,
the plasmids were prepared, and the nucleic acid sequence
of each OspA was determined by the dideoxy chaintermination technique using the Sequenase kit (United
States Biochemical). Directed sequencing was performed
with M13 primers followed by OspA-specific primers derived
from sequences, previously obtained with M13 primers.

Because the 5' and 3' ends of the OspA gene are highly conserved (Fikrig, E.S. et al., J. Immunol. 7:2256-2260

15 (1992); Bergstrom, S. et al., Mol. Microbiol. 3: 479-486 (1989); Zumstein, G. et al., Med. Microbiol. Immunol. 181: 57-70 (1992)), the 5' and 3' primers for cloning can be based upon any known OspA sequences. For example, the following primers based upon the OspA nucleic acid sequence from strain B31 were used:

5'-GGAGAATATATTATGAAA-3' (-12 to +6) (SEQ ID NO. 4); and 5'-CTCCTTATTTTAAAGCG-3' (+826 to +809) (SEQ ID NO. 5). (Schubach, W.H. et al., <u>Infect. Immun 59</u>:1811-1915 (1991)).

OspA genes isolated in this manner include those for strains B31, K48, PGau, and 25015; the nucleic acid sequences are depicted in the sequence listing as SEQ ID NO. 6 (OspA-B31), SEQ ID NO. 8 (OspA-K48), SEQ ID NO. 10 (OspA-PGau), and SEQ ID NO. 12 (OspA-25015). An alignment of these and other OspA nucleic acid sequences is shown in Figure 42. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 7 (OspA-B31), SEQ ID NO. 9 (OspA-K48), SEQ ID NO. 11 (OspA-PGau), and SEQ ID NO. 13 (OspA-25015).

The following primers were used to generate specific nucleic acid sequences of the OspA gene, to be used to

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generate chimeric nucleic acid sequences (as described in Example 4):

- 5'-GTCTGCAAAAACCATGACAAG-3' (plus strand primer #369) (SEQ ID NO. 14);
- 5 5'-GTCATCAACAGAAGAAAAATTC-3' (plus strand primer #357) (SEQ ID NO 15);
  - 5'-CCGGATCCATATGAAAAATATTTATTGGG-3' (plus strand primer #607) (SEQ ID NO. 16);
  - 5'-CCGGGATCCATATGGCTAAGCAAAATGTTAGC-3' (plus strand primer
- 10 #584) (SEQ ID NO. 17);
  - 5'-GCGTTCAAGTACTCCAGA-3' (minus strand primer #200) (SEQ ID NO. 18);
    - 5'-GATATCTAGATCTTATTTTAAAGCGTT-3' (minus strand primer #586) (SEQ ID NO. 19); and
- 15 5'-GGATCCGGTGACCTTTTAAAGCGTTTTTAAT-3' (minus strand primer #1169) (SEQ ID NO. 20).

Cloning and Sequencing of OspB

Similar methods were also used to isolate OspB genes. One OspB genes isolated is represented as SEQ ID NO. 21 (OspB-B31); its encoded amino acid sequence is SEQ ID NO. 22.

The following primers were used to generate specific nucleic acid sequences of the OspB gene, to be used in generation of chimeric nucleic acid sequences (see Example

25 4):

- 5'-GGTACAATTACAGTACAA-3' (plus strand primer #721) (SEQ ID NO. 23);
- 5'-CCGAGAATCTCATATGGCACAAAAAGGTGCTGAGTCAATTGG-3' (plus strand primer #1105) (SEQ ID NO. 24);
- 5'-CCGATATCGGATCCTATTTTAAAGCGTTTTTAAGC-3' (minus strand primer # 1106) (SEQ ID NO. 25); and 5'-GGATCCGGTGACCTTTTAAAGCGTTTTTAAG-3' (minus strand primer #1170) (SEQ ID NO. 26).

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Cloning and Sequencing of OspC

Similar methods were also used to isolate OspC genes. The following primers were used to isolate entire OspC genes from Borrelia strains B31, K48, PKO, and pTrob:

5'-GTGCGCGACCATATGAAAAAGAATACATTAAGTGCG-3' (plus strand primer having Ndel site combined with start codon) (SEQ ID NO. 27), and

5'-GTCGGCGGATCCTTAAGGTTTTTTTGGACTTTCTGC-3' (minus strand primer having BamH1 site followed by stop codon) (SEQ ID NO. 28).

The nucleic acid sequences of the OspC genes were then determined by the dideoxy chain-termination technique using the Sequenase kit (United States Biochemical). OspC genes isolated and sequenced in this manner include those for strains B31, K48, PKo, and Tro; the nucleic acid sequences are depicted in the sequence listing as SEQ ID NO. 29 (OspC-B31), SEQ ID NO. 31 (OspC-K48), SEQ ID NO. 33 (OspC-PKo), and SEQ ID NO. 35 (OspC-Tro). An alignment of these sequences is shown in Figure 38. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 30 (OspC-B31), SEQ ID NO. 32 (OspC-K48), SEQ ID NO. 34 (OspC-PKo), and SEQ ID NO. 36 (OspC-Tro).

Truncated OspC genes were generated using other

25 primers. These primers were designed to amplify nucleic acid sequences, derived from the OspC gene, that lacked the nucleic acids encoding the signal peptidase sequence of the full-length protein. The primers corresponded to bp 58-75 of the natural protein, with a codon for Met-Ala attached

30 ahead. For strain B31, the following primer was used:

5'-GTGCGCGACCATATGGCTAATAATTCAGGGAAAGAT-3' (SEQ ID NO. 37).

For strain PKo,

5'-GTGCGCGACCATATGGCTAGTAATTCAGGGAAAGGT-3' (SEQ ID NO. 38)
35 was used.

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For strains pTrob and K48, 5'-GTGCGCGACCATATGGCTAATAATTCAGGTGGGGAT-3' (SEQ ID NO. 39) was used.

Additional primers were also designed to amplify
nucleic acids encoding particular polypeptides, for use in
creation of chimeric nucleic acid sequences (see Example
4). These primers included:

- 5'-CTTGGAAAATTATTTGAA-3' (plus strand primer #520) (SEQ ID NO. 40);
- 5'-CACGGTCACCCCATGGGAAATAATTCAGGGAAAGG-3' (plus strand
  primer #58) (SEQ ID NO. 41);
  - 5'-TATAGATGACAGCAACGC-3' (minus strand primer #207) (SEQ ID NO. 42); and
- 5'-CCGGTGACCCCATGGTACCAGGTTTTTTTGGACTTTCTGC-3' (minus strand primer #636) (SEQ ID NO. 43).

Cloning and Sequencing of OspD

Similar methods can be used to isolate OspD genes. An alignment of four OspD nucleic acid sequences (from strains pBo, PGau, DK29, and K48) is shown in Figure 39.

20 Cloning and Sequencing of p12

The p12 gene was similarly identified. Primers used to clone the entire p12 gene included: 5'CCGGATCCATATGGTTAAAAAAATAATATTTATTTC-3' (forward primer # 757) (SEQ ID NO. 44); and 5'-

25 GATATCTAGATCTTTAATTGCTCTGCTCACTCTCTTC-3' (reverse primer #758) (SEQ ID NO. 45).

To amplify a truncated p12 gene (one in which the transcribed protein is non-lipidated, and begins at amino acid 18 of the native sequence), the following primers were used: 5'-CCGGGATCCATATGGCTAGTGCAATTGGTCGTGG-3' (forward primer # 759) (SEQ ID NO. 46); and primer #758 (SEQ ID NO. 45).

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Cloning and Sequencing of p41 (fla)

A similar approach was used to clone and sequence genes encoding the p41 (fla) protein. The p41 sequences listed in Table II with GenBank accession numbers were 5 isolated using the following primers from strain B31: 5'-ATGATTATCAATCATAAT-3' (+1 to +18) (SEQ ID NO. 47); and 5'-TCTGAACAATGACAAAAC-3' (+1008 to +991) (SEQ ID NO. 48). The nucleic acid sequences of p41 isolated in this manner are depicted in the sequence listing as SEQ ID NO. 51 (p41-10 PGau), and SEQ ID NO. 53 (p41-DK29). An alignment of several p41 nucleic acid sequences, including those for strains B31, pKa1, PGau, pBo, DK29, and pKo, is shown in Figure 41. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as 15 SEQ ID NO. 50 (p41-K48), SEQ ID NO. 52 (p41-PGau), SEQ ID NO. 54 (p41-DK29), SEQ ID NO. 56 (p41-PTrob), and SEQ ID NO. 58 (p41-PHei).

Other primers were designed to amplify nucleic acid sequences encoding polypeptides of p41, to be used in chimeric nucleic acid sequences. These primers included: 5'-TTGGATCCGGTCACCCCATGGCTCAATATAACCAATG-3' (minus strand primer #122) (SEQ ID NO. 59); 5'-TTGGATCCGGTCACCCCATGGCTTCTCAAAATGTAAG-3' (plus strand

primer # 140) (SEQ ID NO. 60);

5'-TTGGATCCGGTGACCAACTCCGCCTTGAGAAGG-3' (minus strand
primer # 234) (SEQ ID NO. 61); and
5'-TTGGATCCGGTGACCTATTTGAGCATAAGATGC-3' (minus strand
primer #141) (SEQ ID NO. 62).

Cloning and Sequencing of p93

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The same approach was also used to clone and sequence p93 protein. Genes encoding p93, as listed in Table II with GenBank accession numbers, were isolated by this method with the following primers from strain B31:

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5'-GGTGAATTTAGTTGGTAAGG-3' (-54 to -35) (SEQ ID NO. 63);

5'-CACCAGTTTCTTTAAGCTGCTCCTGC-3' (+1117 to +1092) (SEQ ID NO. 64).

The nucleic acid sequences of p93 isolated in this manner are depicted in the sequence listing as SEQ ID NO. 65 (p93-B31), SEQ ID NO. 67 (p93-K48) SEQ ID NO. 69 (p93-PBo), SEQ ID NO. 71 (p93-PTrob), SEQ ID NO. 73 (p93-PGau), SEQ ID NO. 75 (p93-25015), and SEQ ID NO. 77 (p93-PKo).

The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 66 (p93-B31), SEQ ID NO. 68 (p93-K48) SEQ ID NO. 70 (p93-PBo), SEQ ID NO. 72 (p93-PTrob), SEQ ID NO. 74 (p93-PGau), SEQ ID NO. 76 (p93-25015), and SEQ ID NO. 78 (p93-PKo).

Other primers were used to amplify nucleic acid sequences encoding polypeptides of p93 to be used in generating chimeric nucleic acid sequences. These primers included:

5'-CCGGTCACCCCATGGCTGCTTTAAAGTCTTTA-3' (plus strand primer 20 #475) (SEQ ID NO. 79);

5'-CCGGTCACCCCATGAATCTTGATAAAGCTCAG-3' (plus strand primer #900) (SEQ ID NO. 80);

5'-CCGGTCACCCCATGGATGAAAAGCTTTTAAAAAGT-3' (plus strand primer #1168) (SEQ ID NO. 81);

5'-CCGGTCACCCCATGGTTGAGAAATTAGATAAG-3' (plus strand primer #1423) (SEQ ID NO. 82); and 5'-TTGGATCCGGTGACCCTTAACTTTTTTTAAAG-3' (minus strand primer # 2100) (SEQ ID NO. 83).

## C. Expression of Proteins from Borrelia Genes

The nucleic acid sequences described above can be incorporated into expression plasmids, using standard techniques, and transfected into compatible host cells in order to express the proteins encoded by the nucleic acid

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sequences. As an example, the expression the pl2 gene and the isolation of pl2 protein is set forth.

Amplification of the p12 nucleic acid sequence was conducted with primers that included a NdeI restriction 5 site into the nucleic acid sequence. The PCR product was extracted with phenol/chloroform and precipitated with ethanol. The precipitated product was digested and ligated into an expression plasmid as follows: 15  $\mu$ l (approximately 1  $\mu g$ ) of PCR DNA was combined with 2  $\mu l$  10X 10 restriction buffer for NdeI (Gibco/BRL), 1  $\mu$ l NdeI (Gibco/BRL), and 2  $\mu$ l distilled water, and incubated overnight at 37°C. This mixture was subsequently combined with 3  $\mu$ l 10X buffer (buffer 3, New England BioLabs), 1  $\mu$ l BamHI (NEB), and 6  $\mu l$  distilled water, and incubated at 37° 15 for two hours. The resultant material was purified by preparative gel electrophoresis using low melting point agarose, and the band was visualized under long wave ultraviolet light and excised from the gel. The gel slice was treated with Gelase using conditions recommended by the 20 manufacturer (Epicentre Technologies). The resulting DNA pelled was resuspended in 25-50  $\mu l$  of 10 mM TRIS-CL (pH 8.0) and 1 mM EDTA (TE). An aliquot of this material was ligated into the Pet9c expression vector (Dunn, J. J. et al., Protein Expression and Purification 1: 159 (1990)).

To ligate the material into the Pet9c expression vector, 20-50 ng of pl2 nucleic acid sequences cut and purified as described above was combined with 5  $\mu$ l 10 One-Phor-All (OPA) buffer (Pharmacia), 30-60 ng Pet9c cut with NdeI and BamHI, 2.5  $\mu$ l 20 mM ATP, 2  $\mu$ l T4 DNA ligase (Pharmacia) diluted 1:5 in 1% OPA buffer, and sufficient distilled water to bring the final volume to 50  $\mu$ l. The mixture was incubated at 12°C overnight.

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The resultant ligations were transformed into competent DH5-alpha cells and plated on nutrient agar plates containing 50  $\mu g/ml$  kanamycin and incubated

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overnight at 37 °C. DH5-alpha is used as a "storage strain" for T7 expression clones, because it is RecA deficient, so that recombination and concatenation are not problematic, and because it lacks the T7 RNA polymerase gene necessary to express the cloned gene. The use of this strain allows for cloning of potentially toxic gene products while minimizing the chance of deletion and/or rearrangement of the desired genes. Other cell lines having similar properties may also be used.

10 Kanamycin resistant colonies were single-colony purified on nutrient agar plates supplemented with kanamycin at 50  $\mu$ g/ml. A colony from each isolate was inoculated into 3-5 ml of liquid medium containing 50  $\mu$ g/ml kanamycin, and incubated at 37°C without agitation.

15 Plasmid DNA was obtained from 1 ml of each isolate using a hot alkaline lysis procedure (Mantiatis, T. et al., Molecular Cloning: A Laboratory Manual, cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1982)).

Plasmid DNA was digested with EcoRI and BglII in the
following manner: 15 μl plasmid DNA was combined with 2 μl
10X buffer 3 (NEB), 1 μ EcoRI (NEB), 1 μl BglII (NEB) and 1
μl distilled water, and incubated for two hours at 37°C.
The entire reaction mixture was electrophoresed on an
analytical agarose gel. Plasmids carrying the pl2 insert
were identified by the presence of a band corresponding to
925 base-pairs (full length pl2) or 875 base-pairs
(nonlipidated pl2).

One or two plasmid DNAs from the full length and nonlipidated p12 clones in Pet9c were used to transform

30 BL21 DE3 pLysS to kanamycin resistance as described by Studier et al. (Methods in Enzymology, Goeddel, D. (Ed.), Academic Press, 185: 60-89 (1990)). One or two transformants of the full length and nonlipidated clones were single-colony purified on nutrient plates containing

35 25 µg/ml chloramphenicol (to maintain pLysS) and 50 µg/ml

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kanamycin at 37 °C. One colony of each isolate was inoculated into liquid medium supplemented with chloramphenicol and kanamycin and incubated overnight at 37°C. The overnight culture was subcultured the following morning into 500 ml of liquid broth with chloramphenicol (25 μg/ml) and kanamycin (50 μg/ml) and grown with aeration at 37°C in an orbital air-shaker until the absorbance at 600 nm reached 0.4-0.7. Isopropyl-thio-galactoside (IPTG) was added to a final concentration of 0.5 mM, for induction, and the culture was incubated for 3-4 hours at 37° as before. The induced cells were pelleted by centrifugation and resuspended in 25 ml of 20 mM NaPO<sub>4</sub> (pH 7.7). A small aliquot was removed for analysis by gel electrophoresis. Expressing clones produced proteins which migrated at the 12 kDa position.

A crude cell lysate was prepared from the culture as described for recombinant OspA by Dunn, J.J. et al., (Protein Expression and Purification 1: 159 (1990)). crude lysate was first passed over a Q-sepharose column 20 (Pharmacia) which had been pre-equilibrated in Buffer A: 10 mM  $\mathrm{NaPO_4}$  (pH 7.7), 10 mM  $\mathrm{NaCl}$ , 0.5 mM  $\mathrm{PMSF}$ . The column was washed with 10 mM NaPO4, 50 mM NaCl and 0.5 mM PMSF and then pl2 was eluted in 10 mM NaPO4, 0.5 mM PMSF with a NaCl gradient from 50-400 mM. pl2 eluted approximately halfway 25 through the gradient between 100 and 200 mM NaCl. The peak fractions were pooled and dialyzed against 10 mM NaPo4 (pH 7.7), 10 mM NaCl, 0.5 mM PMSF. The protein was then concentrated and applied to a Sephadex G50 gel filtration column of approximately 50 ml bed volume (Pharmacia), in 10 30 mM NaPO, 200 mM NaCl, 0.5 mM PMSF. p12 would typically elute shortly after the excluded volume marker. Peak fractions were determined by running small aliquots of all fractions on a gel. The p12 peak was pooled and stored in small aliquots at -20°C.

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#### Generation of Chimeric Nucleic Acid Example 4. Sequences and Chimeric Proteins

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#### General Protocol for Creation of Chimeric Nucleic Acid <u>A.</u> Sequences

The megaprimer method of site directed mutagenesis and its modification were used to generate chimeric nucleic acid sequences (Sarkar and Sommer, Biotechniques 8(4): 404-407 (1990); Aiyar, A. and J. Leis, <u>Biotechniques 14(3):</u> 366-369 (1993)). A 5' primer for the first genomic 10 template and a 3' fusion oligo are used to amplify the desired region. the fusion primer consists of a 3' end of the first template (DNA that encodes the amino-proximal polypeptide of the fusion protein), coupled to a 5' end of the second template (DNA that encodes the carboxy-proximal 15 polypeptide of the fusion protein).

The PCR amplifications are performed using Taq DNA polymerase, 10X PCR buffer, and MgCl<sub>2</sub> (Promega Corp., Madison, WI), and Ultrapure dNTPs (Pharmacia, Piscataway, NJ). One  $\mu g$  of genomic template 1, 5  $\mu$  of 10  $\mu M$  5' oligo 20 and 5  $\mu$ l of 10  $\mu$ M fusion oligo are combined with the following reagents at indicated final concentrations: 10X Buffer-Mg FREE (1X),  $MgCl_2$  (2 mM), dNTP mix (200  $\mu$ M each dNTP), Taq DNA polymerase (2.5 units), water to bring final volume to 100  $\mu$ l. A Thermal Cycler (Perkin Elmer Cetus,

25 Norwalk, CT) is used to amplify under the following conditions: 35 cycles at 95°C for one minute, 55°C for two minutes, and 72° for three minutes. This procedure results in a "megaprimer".

The resulting megaprimer is run on a 1X TAE, 4% low-30 melt agarose gel. The megaprimer band is cut from the gel and purified using the Promega Magic PCR Preps DNA purification system. Purified megaprimer is then used in a second PCR step. One  $\mu g$  of genomic template 2, approximately 0.5  $\mu g$  of the megaprimer, and 5  $\mu$  of 10  $\mu M$  3'

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oligo are added to a cocktail of 10X buffer, MgCl2, dNTPs and Taq at the same final concentrations as noted above, and brought to 100  $\mu l$  with water. PCR conditions are the same as above. The fusion product resulting from this 5 amplification is also purified using the Promega Magic PCR Preps DNA purification system.

The fusion product is then ligated into TA vector and transformed into E. coli using the Invitrogen (San Diego, CA) TA Cloning Kit. Approximately 50 ng of PCR fusion 10 product is ligated to 50 ng of pCRII vector with 1X Ligation Buffer, 4 units of T4 ligase, and brought to 10 Nl with water. This ligated product mixture is incubated at 12°C overnight (approximately 14 hours). Two  $\mu$ l of the ligation product mixture is added to 50  $\mu l$  competent INC F' 15 cells and 2  $\mu$  beta mercaptoethanol. The cells are then incubated for 30 minutes, followed by heat shock treatment at 42°C for 60 seconds, and an ice quenching for two minutes. 450  $\mu$ l of warmed SOC media is then added to the cells, resulting in a transformed cell culture which is 20 incubated at 37°C for one hour with slight shaking. of the transformed cell culture is plated on LB + 50  $\mu g/\mu l$ ampicillin plates and incubated overnight at 37°C. Single white colonies are picked and added to individual overnight cultures containing 3 ml LB with ampicillin (50  $\mu g/\mu l$ ).

The individual overnight cultures are prepared using Promega's Magic Miniprep DNA purification system. A small amount of the resulting DNA is cut using a restriction digest as a check. DNA sequencing is then performed to check the sequence of the fusion nucleic acid sequence, 30 using the United States Biochemical (Cleveland, OH) Sequenase Version 2.0 DNA sequencing kit. Three to five  $\mu g$ of plasmid DNA is used per reaction. 2  $\mu$ l 2M NaOH/2mM EDTA are added to the DNA, and the volume is brought to 20  $\mu l$ with water. The mixture is then incubated at room 35 temperature for five minutes. 7  $\mu$ l water, 3 $\mu$ l 3M NaAc, 75

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 $\mu$ l EtOH are added. The resultant mixture is mixed by vortex and incubated for ten minutes at -70°C, and then subjected to microfugation. After microfuge for ten minutes, the supernatant is aspirated off, and the pellet 5 is dried in the speed vac for 30 second. 6  $\mu l$  water, 2  $\mu l$ annealing buffer, and 2  $\mu l$  of 10  $\mu M$  of the appropriate oligo is then added. This mixture is incubated for 10 minutes at 37°C and then allowed to stand at room temperature for 10 minutes. Subsequently, 5.5  $\mu$ l of label 10 cocktail (described above) is added to each sample of the mixture, which are incubated at room temperature for an additional five minutes. 3.5  $\mu l$  labeled DNA is then added to each sample which is then incubated for five minutes at 37°C. 4  $\mu$ l stop solution is added to each well. 15 is denatured at 95° for two minutes, and then placed on ice.

Clones with the desired fusion nucleic acid sequences are then recloned in frame in the pEt expression system in the lipidated (full length) and non-lipidated (truncated, 20 i.e., without first 17 amino acids) forms. The product is amplified using restriction sites contained in the PCR primers. The vector and product are cut with the same enzymes and ligated together with T4 ligase. The resultant plasmid is transformed into competent E. coli using 25 standard transformation techniques. Colonies are screened as described earlier and positive clones are transformed into expression cells, such as E. coli BL21, for protein expression with IPTG for induction. The expressed protein in its bacterial culture lysate form and/or purified form 30 is then injected in mice for antibody production. The mice are bled, and the sera collected for agglutination, in vitro growth inhibition, and complement- dependent and independent lysis tests.

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## B. Specific Chimeric Nucleic Acid Sequences

Various chimeric nucleic acid sequences were generated. The nucleic acid sequences are described as encoding polypeptides from Borrelia proteins. The chimeric nucleic acid sequences are produced such that the nucleic acid sequence encoding one polypeptide is in the same reading frame as the nucleic acid sequence encoding the next polypeptide in the chimeric protein sequence encoded by the chimeric nucleic acid sequence. The proteins are listed sequentially (in order of presence of the encoding sequence) in the description of the chimeric nucleic acid sequence consists of bp 1-650 from OspA-1 and bp 651-820 from OspA-2 were sequenced, the sequence of the chimer would include the first 650 base pairs from OspA-1 followed immediately by base pairs 651-820 of OspA-2.

OspA-K48/OspA-PGau A chimer of OspA from strain
K48 (OspA-K48) and OspA from strain PGau (OspA-PGau) was
generated using the method described above. This chimeric
nucleic acid sequence included bp 1-654 from OspA-K48,
followed by bp 655-820 from OspA-PGau. Primers used
included: the amino-terminal sequence of OspA primer #607
(SEQ ID NO. 16); the fusion primer,

5'-AAAGTAGAAGTTTTTGAATCCCATTTTCCAGTTTTTTT-3' (minus strand primer #668-654) (SEQ ID NO. 84); the carboxy-terminal sequence of OspA primer #586 (SEQ ID NO. 19); and the sequence primers #369 (SEQ ID NO. 14) and #357 (SEQ ID NO. 15). The chimeric nucleic acid sequence is presented as SEQ ID NO. 85; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 86.

OspA-B31/OspA-PGau A chimer of OspA from strain B31 (OspA-B31) and OspA from strain PGau (OspA-PGau) was generated

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using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-PGau. Primers used included: the fusion primer,

5 5'-AAAGTAGAAGTTTTTGAATTCCAAGCTGCAGTTTT-3' (minus strand primer #668-651) (SEQ ID NO. 87); and the sequence primer, #369 (SEQ ID NO. 14). The chimeric nucleic acid sequence is presented as SEQ ID NO. 88; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 89.

OspA-B31/OspA-K48 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain K48 (OspA-K48) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-K48. Primers used included: the fusion primer,

primer #671-651) (SEQ ID NO. 90); and the sequence primer, #369 (SEQ ID NO. 14). The chimeric nucleic acid sequence 20 is presented as SEQ ID NO. 91; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 92.

5'-AAAGTGGAAGTTTTTGAATTCCAAGCTGCAGTTTTTTT-3' (minus strand

OspA-B31/OspA-25015 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain 25015 (OspA-25015) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-25015. Primers used included: the fusion primer, 5'-TAAAGTTGAAGTGCCTGCATTCCAAGCTGCAGTTT-3' (SEQ ID NO. 93). The chimeric nucleic acid sequence is presented as SEQ ID NO. 94; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 95.

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OspA-K48/OspA-B31/OspA-K48 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain K48 (OspA-K48) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-570 from OspA-B31, followed by bp 570-651 from OspA-B31, followed by bp 650-820 from OspA-K48. Primers used included: the fusion primer, 5'-CCCCAGATTTTGAAATCTTGCTTAAAACAAC-3' (SEQ ID NO.96); and the sequence primer, #357 (SEQ ID NO.15). The chimeric nucleic acid sequence is presented as SEQ ID NO.97; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO.98.

OspA-B31/OspA-K48/OspA-B31/OspA-K48

from strain B31 (OspA-B31) and OspA from strain K48 (OspA-K48) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-420 from OspA-B31, followed by 420-570 from OspA-K48, followed by bp 570-650 from OspA-B31, followed by bp 651-820 from OspA-K48. Primers used included: the fusion primer, 5'-CAAGTCTGGTTCCAATTTGCTCTTGTTATTAT-3' (minus strand primer #436-420) (SEQ ID NO. 99); and the sequence primer, #357 (SEQ ID NO. 15). The chimeric nucleic acid sequence is presented as SEQ ID NO. 100; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 101.

OspA-B31/OspB-B31 A chimer of OspA and OspB from strain
B31 (OspA-B31, OspB-B31) was generated using the method
described above. The chimeric nucleic acid sequence
included bp 1-651 from OspA-B31, followed by bp 652-820
from OspB-B31. Primers used included: the fusion primer,
5'-GTTAAAGTGCTAGTACTGTCATTCCAAGCTGCAGTTTTTTT-3' (minus
strand primer #740-651) (SEQ ID NO. 102); the carboxyterminal sequence of OspB primer #1106 (SEQ ID NO. 25); and
the sequence primer #357 (SEQ ID NO. 15). The chimeric

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nucleic acid sequence is presented as SEQ ID NO. 103; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 104.

OspA-B31/OspB-B31/OspC-B31 A chimer of OspA, OspB and OspC from strain B31 (OspA-B31, OspB-B31, and OspC-B31) was generated using the method described above. The chimeric nucleic acid sequence included bp 1-650 from OspA-B31, followed by bp 652-820 from OspB-B31, followed by bp 74-630 of OspC-B31. Primers used included: the fusion primer, 5'-TGCAGATGTAATCCCATCCGCCATTTTTAAAGCGTTTTT-3' (SEQ ID NO. 105); and the carboxy-terminal sequence of OspC primer (SEQ ID NO. 28). The chimeric nucleic acid sequence is presented as SEQ ID NO. 106; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 107.

OspC-B31/OspA-B31/OspB-B31 A chimer of OspA, OspB and OspC from strain B31 (OspA-B31, OspB-B31, and OspC-B31) was generated using the method described above. The chimeric nucleic acid sequence included bp 1-630 from OspC-B31, followed by bp 52-650 from OspA-B31, followed by bp 650-820 of OspB-B31. Primers used included: the amino-terminal sequence of OspC primer having SEQ ID NO. 27; the fusion primer, 5'-GCTGCTAACATTTTGCTTAGGTTTTTTTGGACTTTC-3' (minus strand primer #69-630) (SEQ ID NO. 108); and the sequence primers #520 (SEQ ID NO. 40) and #200 (SEQ ID NO. 18). The chimeric nucleic acid sequence is presented as SEQ ID NO. 109; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 110.

# 30 Additional Chimeric Nucleic Acid Sequences

Using the methods described above, other chimeric nucleic acid sequences were produced. These chimeric

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nucleic acid sequences, and the proteins encoded, are summarized in Table 3.

Table III Chimeric Nucleic acid Sequences and the Encoded Proteins

FIOCETIE		
Chimers Generated (base pairs)	SEQ ID NO. (nt)	SEQ ID NO. (protein)
OspA (52-882) / p93 (1168-2100)	111	112
OspB (45-891) / p41 (122-234)	113	114
OspB (45-891) / p41 (122-295)	115	116
OspB (45-891) / p41 (140-234)	117	118
OspB (45-891) / p41 (140-295)	119	120
OspB (45-891) / p41 (122-234) / OspC (58-633)	121	122
OspA-Tro/OspA-Bo	137	138
OspA-PGau/OspA-Bo	139	140
OspA-B31/OspA-PGau/OspA-B31/ OspA-K48	141	142
OspA-PGau/OspA-B31/OspA-K48	143	144

# C. Purification of Proteins Generated by Chimeric Nucleic Acid Sequences

The chimeric nucleic acid sequences described above, as well as chimeric nucleic acid sequences produced by the methods described above, are used to produce chimeric proteins encoded by the nucleic acid sequences. Standard methods, such as those described above in Example 3, concerning the expression of proteins from Borrelia genes, can be used to express the proteins in a compatible host organism. The chimeric proteins can then be isolated and purified using standard techniques.

If the chimeric protein is soluble, it can be purified on a Sepharose column. Insoluble proteins can be solubilized in guanidine and purified on a Ni++ column;

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alternatively, they can be solubilized in 10 mM NaPO<sub>4</sub> with 0.1 - 1% TRIXON X 114, and subsequently purified over an S column (Pharmacia). Lipidated proteins were generally purified by the latter method. Solubility was determined by separating both soluble and insoluble fractions of cell lysate on a 12% PAGE gel, and checking for the localization of the protein by Coomasie staining, or by Western blotting with monoclonal antibodies directed to an antigenic polypeptide of the chimeric protein.

#### 10 Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. such equivalents are intended to be encompassed in the scope of the following claims.

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#### CLAIMS

What is claimed is:

- A chimeric protein comprising two or more antigenic Borrelia polypeptides, wherein the antigenic Borrelia polypeptides which comprise the chimeric protein do not occur naturally in the same protein in Borrelia.
  - 2. The chimeric protein of Claim 1, wherein the antigenic Borrelia polypeptides are from two or more different species of Borrelia.
- The chimeric protein of Claim 2, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
  - 4. The chimeric protein of Claim 3, wherein the antigenic Borrelia polypeptides are from corresponding proteins from two or more different species of Borrelia.
- 5. The chimeric protein of Claim 3, wherein the antigenic
  Borrelia polypeptides are from non-corresponding
  proteins from at least two different species of
  Borrelia.
- The chimeric protein of Claim 1, wherein two or more antigenic Borrelia polypeptides are from the same
   species of Borrelia.

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7. The chimeric protein of Claim 6, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.

- 8. The chimeric protein of Claim 7, wherein the antigenic Borrelia polypeptides are from the same protein.
- 9. The chimeric protein of Claim 6, wherein the antigenic Borrelia polypeptides are from different proteins.
- 10. A chimeric protein comprising two antigenic Borrelia polypeptides flanking a tryptophan residue, wherein the amino-proximal polypeptide consists of a polypeptide that is proximal from the single tryptophan residue of a first outer surface protein of Borrelia, and the carboxy-proximal polypeptide consists of a polypeptide that is distal from the single tryptophan residue of a second outer surface protein of Borrelia.
- 20 11. The chimeric protein of Claim 10, wherein the first and second outer surface proteins are from the same species of *Borrelia*.
- 12. The chimeric protein of Claim 11, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
  - 13. The chimeric protein of Claim 11, wherein the first outer surface protein is outer surface protein B, and

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the second outer surface protein is outer surface protein A.

14. The chimeric protein of Claim 10, wherein the first and second outer surface proteins are from different species of *Borrelia*.

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- 15. The chimeric protein of Claim 14, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 10 16. The chimeric protein of Claim 14, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
- 17. The chimeric protein of Claim 14, wherein the first
  and second outer surface proteins are corresponding
  proteins selected from the group consisting of: outer
  surface protein A and outer surface protein B.
- 18. The chimeric protein of Claim 10, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 19. The chimeric protein of Claim 18, wherein the aminoproximal polypeptide further comprises a first,
  second, and third hypervariable domain, the first
  hypervariable domain consisting of residues 120
  through 140 of outer surface protein A, the second
  hypervariable domain consisting of residues 150
  through 180 of outer surface protein A, and the third

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hypervariable domain consisting of residues 200 through 217 of outer surface protein A.

20. The chimeric protein of Claim 19, wherein the first and second hypervariable domains are derived from outer surface protein A from different species of Borrelia.

- 21. The chimeric protein of Claim 10, further comprising an antigenic Borrelia polypeptide derived from a Borrelia protein selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
- 22. A nucleic acid sequence encoding a chimeric protein comprising two antigenic Borrelia polypeptides, wherein the two antigenic Borrelia polypeptides which comprise the chimeric protein do not occur naturally in the same protein in Borrelia.
- 23. The nucleic acid sequence of Claim 22, wherein the antigenic Borrelia polypeptides are from two or more different species of Borrelia.
- 24. The nucleic acid sequence of Claim 23, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, pl2, p39, p41, p66, and p93.
  - 25. The nucleic acid sequence of Claim 24, wherein the antigenic *Borrelia* polypeptides are from corresponding

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proteins from two or more different species of Borrelia.

26. The nucleic acid sequence of Claim 24, wherein two or more of the antigenic Borrelia polypeptides are from non-corresponding proteins from different species of Borrelia.

- 27. The nucleic acid sequence of Claim 22, wherein two or more antigenic Borrelia polypeptides are from the same species of Borrelia.
- 10 28. The nucleic acid sequence of Claim 27, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
  - 29. The nucleic acid sequence of Claim 28, wherein the antigenic *Borrelia* polypeptides are from the same protein.
- 30. The nucleic acid sequence of Claim 27, wherein the antigenic Borrelia polypeptides are from different proteins.

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31. A nucleic acid sequence encoding a chimeric protein comprising two antigenic Borrelia polypeptides flanking a tryptophan residue, wherein the aminoproximal polypeptide consists of a polypeptide that is proximal from the single tryptophan residue of a first outer surface protein of Borrelia, and the carboxy-proximal polypeptide consists of a polypeptide that is distal from the single tryptophan residue of a second outer surface protein of Borrelia.

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- 10 32. The nucleic acid sequence of Claim 31, wherein the first and second outer surface proteins are from the same species of *Borrelia*.
- 33. The nucleic acid sequence of Claim 32, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
  - 34. The nucleic acid sequence of Claim 32, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
  - 35. The nucleic acid sequence of Claim 31, wherein the first and second outer surface proteins are from different species of Borrelia.
- 36. The nucleic acid sequence of Claim 35, wherein the
  25 first outer surface protein is outer surface protein A
  and the second outer surface protein is outer surface
  protein B.

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- 37. The nucleic acid sequence of Claim 35, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
- 5 38. The nucleic acid sequence of Claim 35, wherein the first and second outer surface proteins are corresponding proteins selected from the group consisting of: outer surface protein A and outer surface protein B.
- 10 39. The nucleic acid sequence of Claim 31, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 40. The nucleic acid sequence of Claim 39, wherein the
  amino-proximal polypeptide further comprises a first
  and a second hypervariable domain, the first
  hypervariable domain consisting of amino acid residues
  1 through 140 of outer surface protein A, and the
  second hypervariable domain consisting of amino acid
  residues 150 through 217 of outer surface protein A.
  - 41. The nucleic acid sequence of Claim 40, wherein the first and second hypervariable domains are derived from outer surface protein A from different species of Borrelia.
- 25 42. The nucleic acid sequence of Claim 31, further comprising an antigenic Borrelia polypeptide derived from a Borrelia protein selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.

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43. A nucleic acid sequence having a sequence selected from the group consisting of: SEQ ID NO. 85, SEQ ID NO. 88, SEQ ID NO. 91, SEQ ID NO. 94, SEQ ID NO. 97, SEQ ID NO. 100, SEQ ID NO. 103, SEQ ID NO. 106, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 141, and SEQ ID NO. 143.

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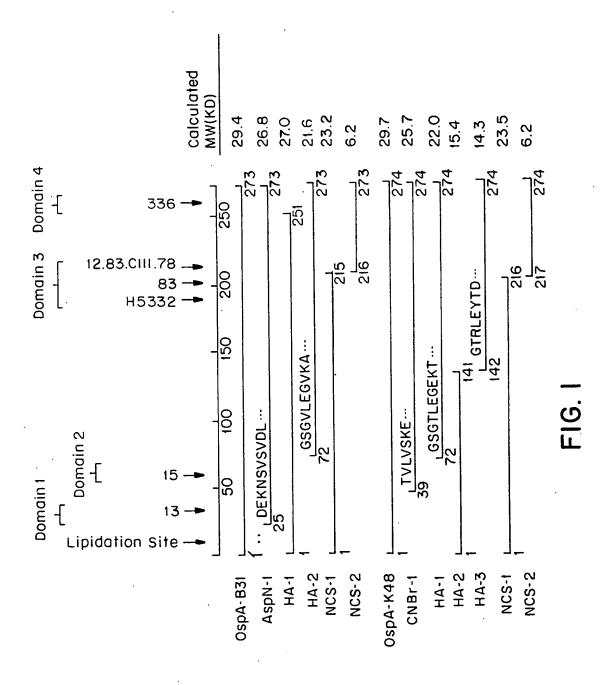
- 44. A protein having an amino acid sequence selected from the group consisting of: SEQ ID NO. 86, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 95, SEQ ID NO. 98, SEQ ID NO. 101, SEQ ID NO. 104, SEQ ID NO. 107, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 138, SEQ ID NO. 140, SEQ ID NO. 142, and SEQ ID NO. 144.
  - 45. A chimeric protein according to any one of claims 1 to 21 and 44 for use in therapy or diagnosis, for example as a vaccine against <u>Borrelia</u> infection, in immunodiagnostic assays to detect the presence of antibodies to <u>Borrelia</u> or to measure T-cell reactivity.
  - 46. A chimeric protein according to claim 45, wherein the immunodiagnostic assay is a dot blot, Western blot, ELISA or agglutination assay.

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- 47. Use of the chimeric protein according to any one of claims 1 to 21 and 44, or the nucleic acid sequence of any one of claims 22 to 43, for the manufacture of a compound for use in therapy or diagnosis, for example as a vaccine against <u>Borrelia</u> infection, in immunodiagnostic assays to detect the presence of antibodies to <u>Borrelia</u> or to measure T-cell reactivity.
- 48. Use according to claim 47, wherein the

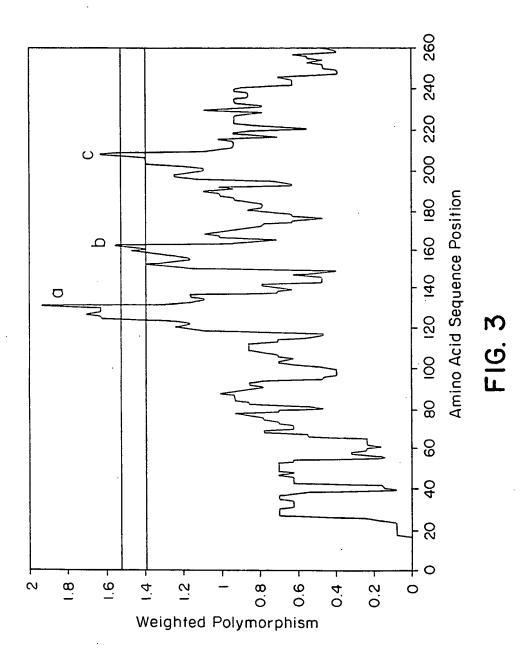
  immunodiagnostic assay is a dot blot, Western blot,

  ELISA or agglutination assay.



				ğ	Domain	-								Domain		~				
	34	35	36	5 37	38	39	40	41		65	99	67	89	69	70	7.1	72	73	74	75
A-B31	ı	4	O	ы	Σ	×	>	IJ	A-B31	ŋ	H	S	Ω	×	z	z	v	တ	ซ	>
A-TRo	า	ď	Ö	M	Σ	×	>	Ţ	A-TRO	ט	F	ຜ	D	×	တ	z	r	ຜ	U	H
A-K48	ы	Д	Ö	ט	Σ	H	>	ı	A-K48	ტ	H	ຜ	Ω	×	z	z	U	S	ט	H
A-DK29	'n	Д	Ŋ	ტ	Σ	۲	>	ı	A-DK29	ซ	Ħ	S	Ω	×	z	z	U	ß	v	H
A-P/Gau	IJ	ሷ	Ö	ы	Σ	×	>	ם	A-P/Gau	Ö	H	ຶ່	Д	×	Д	z	ט	S	ט	H
A-PKo	1	ሷ	ט	Œ	Σ	×	>	'n	A-PKo	v	H	S	Ω	×	Ω	z	Ö	တ	ซ	Ę÷
A-IP3	'n	Д	O	E	н	×	>	ı	A-IP3	ტ	Ħ	ຜ	Ω	×	Ω	z	ט	S	<sub>O</sub>	>
A-IP90	ı	գ	Ö	ט	Σ	O	>	יז	A-IP90	ט	H	ຜ	Д	×	z	z	ט	S	v	H
A-25015		α	U	យ	Σ	×	>	J.	A-25015	ט	Ŧ	S	Ω	×	z	<b>Z</b>	Ö	S	ຶ	>
			ы	Domain 3	m							Domain 4	ln 4							
	190		(4	200		210		220		250		260		270						
A-B31	NI	SKSG	EVS	NISKSGEVSVELNDTDSSAATKKTAAWNSGT	TDSSA	ATKK	TAAK	INSGT	A-B31	SNGTKLEGSAVEITKLDEIKN	LEGS.	AVEI	rkld!	EIKN						
A-TRO	HII	:NSC	EIT	hipnsgeitvelndsnstqatkktgkwdsnt	SNSTÇ	<b>ATKK</b>	TGKE	DSNT	A-TRO	SAGINLEGNAVEIKTLDELKN	LEGN	AVEI	KTLDI	ELKN						
A-K48	NII	LKSG	EIT	NILKSGEITVALDDSDTTQATKKTGKWDSKT	SDTTC	ATKK	TGKW	DSKT	A-K48	SAGTNLEGKAVEITTLKELKN	LEGK	AVEI	LTLKI	ELKN						
A-DK29	NII	ZKSG	EIT	ALDD	SDTT	MTKK	TGKW	DSKT	A-DK29	SAGTNLEGKAVEITTLKELKN	EGK	AVEI:	LTLKI	ELKN						
A-P/Gau	EI	<b>AKSGI</b>	EVI	Elaksgevtvalndtnttoatkktgamdskt	TINT	ATKK	TGAM	DSKT	A-P/Gau	SAGTNLEGTAVEIKTLDELKN	LEGI	AVEI	KTLDI	ELKN						
A-PKo	EI	AKSGI	EVI	ELAKSGEVTVALNDTNTTQATKKTGAMDSKT	TITLE	ATKK	TGAW	DSKT	A-PKo	SAGTNLEGTAVEIKTLDELKN	LEGI	AVEI	KTLD	ELKN						
A-IP3	EI	<b>AKSG</b>	FYE	Elaksgevtvalndtnttqatkktgawdskt	TINIT	ATKK	TGAW	DSKT	A-IP3	SAGTNLEGTAVEIKTLDELKN	LEGI	AVEI	KTLDI	ELKN						
A-IP90	HIS	SNSG	EIT	HISNSGEITVELNDSDTTQATKKTGTWDSKT	SDTTC	ATKK	TGTW	DSKT	A-1P90	SAGTNLEGKAVEITTLKELKN	LEGK	AVEI	LTLK	ELKN						
A-25015	HIS	SKSGI	EVT	LELIND'	TDSTÇ	ATKK	TGKW	DAGT	A-25015	SAGTNLEGTAVEIKTLDEIKN	EGT	AVEI	KTLDI	EIKN						

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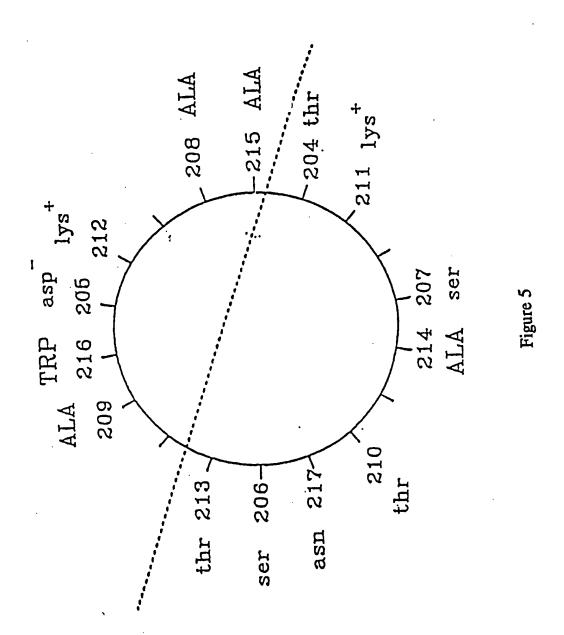
SUBSTITUTE SHEET (RULE 26)

K48: ALDDSDTTQATKKTGKWDSKT
613: ELNDSDISAATKKTAAWNSGT
625: ELNDTDSSAATKKTGKWNSGT
640: ELNDTDSSAATKKTAAWDSKT
613/625: ELNDSDISAATKKTGKWNSGT
613/640: ELNDSDISAATKKTAAWDSKT

ELNDTDSSAATKKTAAWNSGT

B31:

Figure 4



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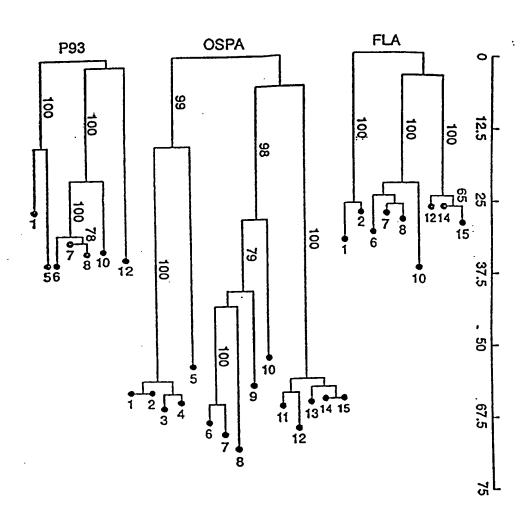


Figure 6

ATG Met 1	AAA Lys	AAA Lys	TAT Tyr	TTA Leu 5	TTG Leu	GGA Gly	ATA Ile	GGT Gly	CTA Leu 10	ATA Ile	TTA Leu	GCC Ala	TTA Leu	ATA Ile 15	GCA Ala	48
TGT Cys	AAG Lys	CAA Gln	AAT Asn 20	GTT Val	AGC Ser	AGC Ser	CTT Leu	GAC Asp 25	GAG Glu	AAA Lys	AAC Asn	AGC Ser	GTT Val 30	TCA Ser	GTA Val	<b>96</b>
				GAA Glu												144
				GAT Asp												192
				AAA Lys												240
GCT Ala	GAC Asp	AAA Lys	AGT Ser	AAA Lys 85	GTA Val	AAA Lys	TTA Leu	ACA Thr	ATT Ile 90	TCT Ser	GAC Asp	GAT Asp	CTA Leu	GGT Gly 95	CAA Gln	288
				GTT Val											AAA Lys	336
				AAA Lys												384
				TCT Ser												432
				GGA Gly												480
				TAT Tyr 165				Gly				_				528
-				AAA Lys								Lys				576
				GTT Val												624

Figure 7 (1 of 2)

		Lys					Thr 220			672
							GTG Val			720
							GGC Gly			768
							ATT Ile			816
AAA	TA									822

Figure 7 (2 of 2)

140

OSPA K48

ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TIT TIT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala> 60 70 80 90 50 TGT AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA AAT AGC GTT TCA GTA ACA TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTA TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val>

120 100 110 GAT TTA CCT GGT GGA ATG ACA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTA AAT GGA CCA CCT TAC TGT CAA GAA CAT TCA TTT CTT TTT CTG TTT Asp Leu Pro Gly Gly Met Thr Val Leu Val Ser Lys Glu Lys Asp Lys>

170 180 150 160 GAC GGT AAA TAC AGT CTA GAG GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCA TTT ATG TCA GAT CTC CGT TGT CAT CTG TTC GAA CTC GAA TTT Asp Gly Lys Tyr Ser Leu Glu Ala Thr Val Asp Lys Leu Glu Leu Lys>

230 220 240 200 210 GGA ACT TCT GAT AAA AAC AAC GGT TCT GGA ACA CTT GAA GGT GAA AAA CCT TGA AGA CTA TTT TTG TTG CCA AGA CCT TGT GAA CTT CCA CTT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Thr Leu Glu Gly Glu Lys>

260 270 250

ACT GAC AAA AGT AAA GTA AAA TTA ACA ATT GCT GAT GAC CTA AGT CAA TGA CTG TTT TCA TTT CAT TTT AAT TGT TAA CGA CTA CTG GAT TCA GTT Thr Asp Lys Ser Lys Val Lys Leu Thr Ile Ala Asp Asp Leu Ser Gln>

300 310 320 330

ACT AAA TTT GAA ATT TTC AAA GAA GAT GCC AAA ACA TTA GTA TCA AAA TGA TTT AAA CTT TAA AAG TTT CTT CTA CGG TTT TGT AAT CAT AGT TTT Thr Lys Phe Glu Ile Phe Lys Glu Asp Ala Lys Thr Leu Val Ser Lys>

350 360 370 380 340

AAA GTA ACC CTT AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAC GAA TTT CAT TGG GAA TTT CTG TTC AGT AGT TGT CTT CTT TTT AAG TTG CTT Lys Val Thr Leu Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu>

FIGURE 8 (1 of 3)

OSP A K48

400 420 430 390 AAG GGT GAA ACA TCT GAA AAA ACA ATA GTA AGA GCA AAT GGA ACC AGA TTC CCA CTT TGT AGA CTT TTT TGT TAT CAT TCT CGT TTA CCT TGG TCT Lys Gly Glu Thr Ser Glu Lys Thr Ile Val Arg Ala Asn Gly Thr Arg> 470 450 460 480 440 CTT GAA TAC ACA GAC ATA AAA AGC GAT GGA TCC GGA AAA GCT AAA GAA GAA CTT ATG TGT CTG TAT TTT TCG CTA CCT AGG CCT TTT CGA TTT CTT Leu Glu Tyr Thr Asp Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu> 510 500 520 490 GTT TTA AAA GAC TTT ACT CTT GAA GGA ACT CTA GCT GCT GAC GGC AAA CAA AAT TIT CTG AAA TGA GAA CTT CCT TGA GAT CGA CGA CTG CCG TIT Val Leu Lys Asp Phe Thr Leu Glu Gly Thr Leu Ala Ala Asp Gly Lys> 530 540 550 560 ACA ACA TTG AAA GTT ACA GAA GGC ACT GTT GTT TTA AGC AAG AAC ATT TGT TGT AAC TTT CAA TGT CTT CCG TGA CAA CAA AAT TCG TTC TTG TAA Thr Thr Leu Lys Val Thr Glu Gly Thr Val Val Leu Ser Lys Asn Ile> 600 610 620 580 590 TTA AAA TCC GGA GAA ATA ACA GTT GCA CTT GAT GAC TCT GAC ACT ACT AAT TTT AGG CCT CTT TAT TGT CAA CGT GAA CTG AGA CTG TGA TGA Leu Lys Ser Gly Glu Ile Thr Val Ala Leu Asp Asp Ser Asp Thr Thr> 660 630 640 650 CAG GCT ACT AAA AAA ACT GGA AAA TGG GAT TCA AAA ACT TCC ACT TTA GTC CGA TGA TTT TTT TGA CCT TTT ACC CTA AGT TTT TGA AGG TGA AAT Gln Ala Thr Lys Lys Thr Gly Lys Trp Asp Ser Lys Thr Ser Thr Leu> 690 700 680 710 720 ACA ATT AGT GTG AAT AGC CAA AAA ACC CTT GTA TTC ACA AAA TGT TAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT Thr Ile Ser Val Asn Ser Gln Lys Thr Lys Asn Leu Val Phe Thr Lys> 750 GAA GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA CTT CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT Glu Asp Thr Ile Thr Val Gln Lys Tyr Asp Ser Ala Gly Thr Asn Leu>

Osp A K-48

770 780 790 800 810

GAA GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT
CTT CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA
Glu Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala>

OSP A K48

820 TTA AAA TAA AAT TTT ATT Leu Lys \*\*\*>

FIGURE 8 (3 of 3)

## OSP A PGAU

	10	20	•		30			4	0		
•	• •	•	•	•	•		•		•	•	
ATG AAA AA	A TAT TTA	TTG GGA	ATA (	GGT (	TA A	ATA :	TTA (	GCC	TTA	ATA	GCA
TAC TTT TT Met Lys Ly	T ATA AAT	TAU GIV	The (	Slv I	Leu :	Ile I	Leu .	Ala	Leu	Ile	Ala>
wer bys by	s lyl Deu	Dea Oxy									
50	60	•	70		1	В0			90		
• •	•	•	*	•		•		•	•	<b></b>	* •
TGC AAG CA	A AAT GTT	AGC AGC	CIT	GAT (	CAA:	ጸጸፉ <i>፣</i> ጉጉጉ '	AAC . TTG :	AGC TCG	CCA	ACT	CIA Cat
Cys Lys Gl	n Asn Val	Ser Ser	Leu	Asp (	Glu :	Lys .	Asn	Ser	Ala	Ser	Val>
cys bys or				•		_					
100	110		120			13	0	_	1	40	
GAT TTG CC			• •	Силт ,	• ሮሞአ	እርጥ	* * * * * * * * * * * * * * * * * * * *	689		CAC.	አአአ
CTA AAC GO	T GGT GAG	TAC TTT	CAA	GAA (	CAT	TCA	TTT	CTT	TTT	CTG	TTT
Asp Leu Pr	o Gly Glu	Met Lys	Val	Leu '	Val	Ser	Lys	Glu	Lys	Asp	Lys>
•	-										
150	1	60	1	70		•	180			19	0
CAC GGT A	G TAC AGT	CTA AAG	GCA	ACA (	GTA	GAC	AAG	ATT	GAG	CTA	AAA
CTG CCA TI	C ATG TCA	GAT TTC	CGT	TGT	CAT	CTG	TTC	AAT	CTC	GAT	TTT
Asp Gly Ly	s Tyr Ser	Leu Lys	Ala	Thr	Val	Asp	Lys	Ile	Glu	Leu	Lys>
200		210		22	•		2	30			240
200	) • •	210	•	22	*	•		•		•	
GGA ACT TO	T GAT AAA	GAC AAT	GGT	TCT	GGA	GTG	CTT	GAA	GGT	ACA	AAA
CCT TGA A	A CTA TTT	CTG TTA	CCA	AGA	CCT	CAC	GAA	CTT	CCA	TGT	TTT
Gly Thr S	er Asp Lys	Asp Asr	Gly	Ser	Gly	Val	Leu	Glu	GIA	Thr	Lys>
	250	260			270.			. 21	80		
•	• •	•		•	•		•		•	•	
GAT GAC A	aa agt aaa	GCA AA	ATTA	ACA	ATT	GCT	GAC	GAT	CTA	AGT	AAA
CTA CTG T	TT TCA TTT ys Ser Lys	CGT TT	TAA	TGT	TAA	CGA	Acn	Acn	GAT	TCA	INSS
Asp Asp L	A2 Set rA2	Mid Dy:	, Leu	1.11	116	A14	vəħ	Jen	Deu	501	<b>0</b> , 0.
290	300	:	310		:	320			330		
• •	•	•	• •	•				•	•	<b>m</b> c.	•
ACC ACA T	TC GAA CTT AG CTT GAA	TTA AA	R GAA T CTT	CTA	CCC	AAA	TGT	TTA	CAC	AGT	TCT
Thr Thr P	he Glu Lev	Leu Ly	s Glu	Asp	Gly	Lys	Thr	Leu	Val	Ser	Arg>
				-	_	_					
340	350	_	360		_	3	70	_		380	
•	GT TCT AG	• • GDC DD	* מרמ	TCA	ACA	таэ	CAA	ATG	ተጥ	- TAA '	GAA
TTT CAT T	CA AGA TC	CTG TT	T TGT	AGT	TGT	CTA	CTT	TAC	AAG	TTA	CTT
Lys Val S	er Ser Arg	Asp Ly	s Thr	Ser	Thr	Asp	Glu	Met	Phe	Asn	Glus

FIGURE 9 (1 of 3)

OSP A PGAU

420 400 · 410 390 AAA GGT GAA TTG TCT GCA AAA ACC ATG ACA AGA GAA AAT GGA ACC AAA TIT CCA CIT AAC AGA CGT TIT TGG TAC TGT TCT CIT TTA CCT TGG TIT Lys Gly Glu Leu Ser Ala Lys Thr Het Thr Arg Glu Asn Gly Thr Lys> 480 450 460 470 440 CTT GAA TAT ACA GAA ATG AAA AGC GAT GGA ACC GGA AAA GCT AAA GAA GAA CTT ATA TGT CTT TAC TTT TCG CTA CCT TGG CCT TTT CGA TTT CTT Leu Glu Tyr Thr Glu Met Lys Ser Asp Gly Thr Gly Lys Ala Lys Glu> 510 500 490 GTT TTA AAA AAG TTT ACT CTT GAA GGA AAA GTA GCT AAT GAT AAA GTA CAA AAT TIT TIC AAA TGA GAA CIT CCT TIT CAT CGA TTA CTA TIT CAT Val Leu Lys Lys Phe Thr Leu Glu Gly Lys Val Ala Asn Asp Lys Val> 550 560 540 ACA TTG GAA GTA AAA GAA GGA ACC GTT ACT TTA AGT AAG GAA ATT GCA TGT AAC CTT CAT TTT CTT CCT TGG CAA TGA AAT TCA TTC CTT TAA CGT Thr Leu Glu Val Lys Glu Gly Thr Val Thr Leu Ser Lys Glu Ile Ala> 600 610 590 AAA TCT GGA GAA GTA ACA GTT GCT CTT AAT GAC ACT AAC ACT ACT CAG TTT AGA CCT CTT CAT TGT CAA CGA GAA TTA CTG TGA TTG TGA TGA GTC Lys Ser Gly Glu Val Thr Val Ala Leu Asn Asp Thr Asn Thr Thr Gln> 650 660 640 630 GCT ACT AAA AAA ACT GGC GCA TGG GAT TCA AAA ACT TCT ACT TTA ACA CGA TGA TTT TTT TGA CCG CGT ACC CTA AGT TTT TGA AGA TGA AAT TGT Ala Thr Lys Lys Thr Gly Ala Trp Asp Ser Lys Thr Ser Thr Leu Thr> 680 ... 700 690 710 ATT AGT GTT AAC AGC AAA AAA ACT ACA CAA CTT GTG TTT ACT AAA CAA TAA TCA CAA TTG TCG TTT TTT TGA TGT GTT GAA CAC AAA TGA TTT GTT Ile Ser Val Asn Ser Lys Lys Thr Thr Gln Leu Val Phe Thr Lys Gln> 730 750 760 TAC ACA ATA ACT GTA AAA CAA TAC GAC TCC GCA GGT ACC AAT TTA GAA ATG TGT TAT TGA CAT TTT GTT ATG CTG AGG CGT CCA TGG TTA AAT CTT. Tyr Thr Ile Thr Val Lys Gln Tyr Asp Ser Ala Gly Thr Asn Leu Glu>

OSP A PGAU

770 780 790 800 810

GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT TTA

CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA AAT

Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asn Ala Leu>

820
AAA TAA
TTT ATT
Lys \*\*\*>

FIGURE 9 (3 of 3)

ATG Met 1	AAA Lys	AAA Lys	TAT Tyr	TTA Leu 5	TTG Leu	GGA Gly	ATA Ile	GGT Gly	CTA Leu 10	ATA Ile	TTA Leu	GCT Ala	TTA Leu	ATA Ile 15	GCA Ala	48
TGT Cys	AAG Lys	CAA Gln	AAT Asn 20	GTT Val	AGC Ser	AGC Ser	CTT Leu	GAC Asp 25	GAG Glu	AAA Lys	AAC Asn	AGC Ser	GTT Val 30	TCA Ser	GTA Val	96
GAT Asp	TTG Leu	CCT Pro 35	GGT Gly	GAA Glu	ATG Met	AAA Lys	GTT Val 40	CTT Leu	GTA Val	AGC Ser	AAA Lys	GAA Glu 45	AAA Lys	GAC Asp	AAA Lys	144
GAC Asp	GGC Gly 50	AAG Lys	TAC Tyr	AGT Ser	CTA Leu	ATG Met 55	GCA Ala	ACA Thr	GTA Val	GAC Asp	AAG Lys 60	CTT Leu	GAG Glu	CTT Leu	AAA Lys	192

Figure 10 (1 of 2)

#### 16/133 /

GGA	ACA	TCT	GAT	AAA Lve	AAC	AAT	GGA Glv	TCT Ser	GGG Glv	GTG Val	CTT Leu	GAA Glu	GGC Gly	GTA Val	AAA Lys	240
65 65	Int	367	nop	_,_	70		,			75					80	
GCT Ala	GAC Asp	AAA Lys	AGC Ser	AAA Lys 85	GTA Val	AAA Lys	TTA Leu	ACA Thr	GTT Val 90	TCT Ser	GAC Asp	GAT Asp	CTÀ Leu	AGC Ser 95	ACA Thr	288
ACC Thr	ACA Thr	CTT Leu	GAA Glu 100	GTT Val	TTA Leu	AAA Lys	GAA Glu	GAT Asp 105	GGC Gly	AAA Lys	ACA Thr	TTA Leu	GTG Val 110	TCA Ser	AAA Lys	336
AAA Lys	AGA Arg	ACT Thr 115	TCT Ser	AAA Lys	GAT Așp	AAG Lys	TCA Ser 120	TCA Ser	ACA Thr	GAA Glu	GAA Glu	AAG Lys 125	TTC Phe	AAT Asn	GAA Glu	. 384
AAA Lys	GGC Gly 130	GAA Glu	TTA Leu	GTT Val	GAA Glu	AAA Lys 135	Ile	ATG Met	GCA Ala	AGA Arg	GCA Ala 140	Man	GGA Gly	ACC Thr	ATA Ile	432
CTT Leu 145	Glu	TAC Tyr	ACA Thr	GGA Gly	ATT Ile 150	. Lys	AGC Ser	GAT Asp	GGA Gly	TCC Ser 155	GGA Gly	AAA Lys	GCT Ala	AAA Lys	GAA Glu 160	480
ACT Thr	TTA Leu	AAA Lys	GAA Glu	TAT Tyr 165	Val	CTT Leu	GAA Glu	GGA Gly	ACT Thr 170	Leu	ACT Thr	GCT Ala	GAA Glu	AAA Lys 175	GCA Ala	528
ACA Thr	TTG	GTG Val	GTT Val 180	. Lys	GAA Glu	GGA Gly	ACT Thr	GTT Val 185	rnr	TTA Leu	AGT	LYS	CAC His 190	110	TCA Ser	576
AAA Lys	TCT Ser	GGA Gly 195	Glu	GTA Val	ACA Thr	GCT Ala	GAA Glu 200	Leu	AAT Asn	GAC Asp	ACT Thr	GAC ABP 205	Jer	ACI	CAA Gln	624
GCT Ala	ACI Thr 210	: Lys	AAA Lys	ACT Thi	GGG Gly	AAA Lys 215	Tr	GAT Asp	GCA Ala	GGC Gly	ACT Thr 220	Ser	ACT Thr	TT?	ACA Thr	672
ATT 116 225	Thr	GTA Val	AA A	AAC ASI	AAA Lys 230	5 Lys	A ACT	Lys	A GCC	CTI Lev 235	ı va.	A TTT	r ACA Thr	AAI Lyi	CAA Gln 240	720
GA(	C ACA	ATT	ACI Thi	A TCI	c Gl	A AAJ	TAC Ty	C GAG	C TC/ p Ser 250	. AT	A GGI	A ACC	C AAC c Asi	25:	G GAA 1 Glu 5	768
GG( Gl <sub>2</sub>	ACI Thi	A GCI	A GT a Va: 26	l Gl	A AT	r AAI e Ly:	A AC	A CT r Le 26	u AB]	r GAI p Gl	A CT	T AA	A AAG 6 Asi 270		r TTA a Leu	816
AG! Ar																. 819

Figure 10 (2 of 2)

430

420

OSP B B-31 Sequence Range: 1 to 891

30 20 10 ATG AGA TTA TTA ATA GGA TTT GCT TTA GCG TTA GCT TTA ATA GGA TGT TAC TOT AAT AAT TAT COT AAA CGA AAT CGC AAT CGA AAT TAT COT ACA Met Arg Leu Leu Ile Gly Phe Ala Leu Ala Leu Ile Gly Cys> 90 80 70 60 • GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT Ala Glm Lys Gly Ala Glu Ser Ile Gly Ser Glm Lys Glu Asm Asp Leu> 130 120 110 100 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG Asn Leu Glu Asp Ser Ser Lys Lys Ser His Gln Asn Ala Lys Gln Asp> 150 170 160 150 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT Leu Pro Ala Val Thr Glu Asp Ser Val Ser Leu Phe Asm Gly Asm Lys> 240 230 220 210 200 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT Ile Phe Val Ser Lys Glu Lys Asn Ser Ser Gly Lys Tyr Asp Leu Arg> 260 270 250 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA Ala Thr Ile Asp Gln Val Glu Leu Lys Gly Thr Ser Asp Lys Asn Asn> 310 320 300 290 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT Gly Ser Gly Thr Leu Glu Gly Ser Lys Pro Asp Lys Ser Lys Val Lys> 370 360 350 340 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA Leu Thr Val Ser Ala Asp Leu Asn Thr Val Thr Leu Glu Ala Phe Asp>

410

400

390

GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT Ala Ser Asn Gln Lys Ile Ser Ser Lys Val Thr Lys Lys Gln Gly Ser> 470 460 450 ATA ACA GAG GAA ACT CTC AAA GCT AAT AAA TTA GAC TCA AAG AAA TTA TAT TGT CTC CTT TGA GAG TTT CGA TTA TTT AAT CTG AGT TTC TTT AAT Ile Thr Glu Glu Thr Leu Lys Ala Asn Lys Leu Asp Ser Lys Lys Leu> 500 510 490 ·**\_**• ACA AGA TCA AAC GGA ACT ACA CTT GAA TAC TCA CAA ATA ACA GAT GCT TGT TCT AGT TTG CCT TGA TGT GAA CTT ATG AGT GTT TAT TGT CTA CGA Thr Arg Ser Asn Gly Thr Thr Leu Glu Tyr Ser Gln Ile Thr Asp Ala> 570 560 550 540 530 GAC AAT GCT ACA AAA GCA GTA GAA ACT CTA AAA AAT AGC ATT AAG CTT CTG TTA CGA TGT TTT CGT CAT CTT TGA GAT TTT TTA TCG TAA TTC GAA Asp Asn Ala Thr Lys Ala Val Glu Thr Leu Lys Asn Ser Ile Lys Leu> 600 590 580 GAA GGA AGT CTT GTA GTC GGA AAA ACA ACA GTG GAA ATT AAA GAA GGT CTT CCT TCA GAA CAT CAG CCT TTT TGT TGT CAC CTT TAA TTT CTT CCA Glu Gly Ser Leu Val Val Gly Lys Thr Thr Val Glu Ile Lys Gl: Gly> 650 660 640 630 ACT GTT ACT CTA AAA AGA GAA ATT GAA AAA GAT GGA AAA GTA AAA GTC TGA CAA TGA GAT TTT TCT CTT TAA CTT TTT CTA CCT TTT CAT TTT CAG Thr Val Thr Leu Lys Arg Glu Ile Glu Lys Asp Gly Lys Val Lys Val> 700 710 690 680 TTT TTG AAT GAC ACT GCA GGT TCT AAC AAA AAA ACA GGT AAA TGG GAA AAA AAC TTA CTG TGA CGT CCA AGA TTG TTT TTT TGT CCA TTT ACC CTT Phe Leu Asn Asp Thr Ala Gly Ser Asn Lys Lys Thr Gly Lys Trp Glu> 750 740 730 GAC AGT ACT AGC ACT TTA ACA ATT AGT GCT GAC AGC AAA AAA ACT AAA CTG TCA TGA TCG TGA AAT TGT TAA TCA CGA CTG TCG TTT TTT TGA TTT Asp Ser Thr Ser Thr Leu Thr Ile Ser Ala Asp Ser Lys Lys Thr Lys> 800 810 790 780 GAT TTG GTG TTC TTA ACA GAT GGT ACA ATT ACA GTA CAA CAA TAC AAC CTA AAC CAC AAG AAT TGT CTA CCA TGT TAA TGT CAT GTT ATG TTG Asp Leu Val Phe Leu Thr Asp Gly Thr Ile Thr Val Gln Gln Tyr Asn>

820 830 840 850 860

ACA GCT GGA ACC AGC CTA GAA GGA TCA GCA AGT GAA ATT AAA AAT CTT TGT CGA CCT TGG TCG GAT CTT CCT AGT CGT TCA CTT TAA TTT TTA GAA Thr Ala Gly Thr Ser Leu Glu Gly Ser Ala Ser Glu Ile Lys Asn Leu>

870 880 890

TCA GAG CTT AAA AAC GCT TTA AAA TAA AGT CTC GAA TTT TTG CGA AAT TTT ATT Ser Glu Leu Lys Asn Ala Leu Lys \*\*\*>

OspC-B31

Sequence Range: 1 to 633

10 20 30 40

ATG AAA AAG AAT ACA TTA AGT GCG ATA TTA ATG ACT TTA TTT TTA TTT TAC TTA TTT TTC TTA TGT AAT TCA CGC TAT AAT TAC TGA AAT AAA AAT AAA MET Lys Lys Asn Thr Leu Ser Ala Ile Leu Met Thr Leu Phe Leu Phe>

50 60 70 80 90

ATA TCT TGT AAT AAT TCA GGG AAA GAT GGG AAT ACA TCT GCA AAT TCT TAT AGA ACA TTA TTA AGT CCC TTT CTA CCC TTA TGT AGA CGT TTA AGA Ile Ser Cys Asn Asn Ser Gly Lys Asp Gly Asn Thr Ser Ala Asn Ser>

100 110 120 130 140

GCT GAT GAG TCT GTT AAA GGG CCT AAT CTT ACA GAA ATA AGT AAA AAA CGA CTA CTC AGA CAA TTT CCC GGA TTA GAA TGT CTT TAT TCA TTT TTT Ala Asp Glu Ser Val Lys Gly Pro Asn Leu Thr Glu Ile Ser Lys Lys>

150 160 170 180 190

ATT ACG GAT TCT AAT GCG GTT TTA CTT GCT GTG AAA GAG GTT GAA GCG TAA TGC CTA AGA TTA CGC CAA AAT GAA CGA CAC TTT CTC CAA CTT CGC Ile Thr Asp Ser Asn Ala Val Leu Leu Ala Val Lys Glu Val Glu Ala>

200 210 220 230 240

TTG CTG TCA TCT ATA GAT GAA ATT GCT GCT AAA GCT ATT GGT AAA AAA AAC GAC AGT AGA TAT CTA CTT TAA CGA CGA TTT CGA TAA CCA TTT TTT Leu Leu Ser Ser Ile Asp Glu Ile Ala Ala Lys Ala Ile Gly Lys Lys>

250 260 270 280

ATA CAC CAA AAT AAT GGT TTG GAT ACC GAA TAT AAT CAC AAT GGA TCA TAT GTG GTT TTA TTA CCA AAC CTA TGG CTT ATA TTA GTG TTA CCT AGT Ile His Gln Asn Asn Gly Leu Asp Thr Glu Tyr Asn His Asn Gly Ser>

290 300 310 320 330

TTG TTA GCG GGA CGT TAT GCA ATA TCA ACC CTA ATA AAA CAA AAA TTA AAC AAT CGC CCT GCA ATA CGT TAT AGT TGG GAT TAT TTT GTT TTT AAT Leu Leu Ala Gly Arg Tyr Ala Ile Ser Thr Leu Ile Lys Gln Lys Leu>

340 350 360 370 380

OspC-B31

Lys Pro \*\*\*>

430 420 400 390 AAA TGT TCT GAA ACA ITT ACT AAT AAA TTA AAA GAA AAA CAC ACA GAT TTT ACA AGA CTT TGT AAA TGA TTA TTT AAT TTT CTT TTT GTG TGT CTA Lys Cys Ser Glu Thr Phe Thr Asn Lys Leu Lys Glu Lys His Thr Asp> 450 CTT GGT AAA GAA GGT GTT ACT GAT GCT GAT GCA AAA GAA GCC ATT TTA GAA CCA TTT CTT CCA CAA TGA CTA CGA CTA CGT TTT CTT CGG TAA AAT Leu Gly Lys Glu Gly Val Thr Asp Ala Asp Ala Lys Glu Ala Ile Leu> 510 --- . 500 490 AAA ACA AAT GGT ACT AAA ACT AAA GGT GCT GAA GAA CTT GGA AAA TTA TTT TGT TTA CCA TGA TTT TGA TTT CCA CGA CTT CTT GAA CCT TTT AAT Lys Thr Asn Gly Thr Lys Thr Lys Gly Ala Glu Glu Leu Gly Lys Leu> 570 550 560 540 530 TTT GAA TCA GTA GAG GTC TTG TCA AAA GCA GCT AAA GAG ATG CTT GCT AAA CTT AGT CAT CTC CAG AAC AGT TTT CGT CGA TTT CTC TAC GAA CGA Phe Glu Ser Val Glu Val Leu Ser Lys Ala Ala Lys Glu Met Leu Ala> 620 610 600 580 590 AAT TCA GTT AAA GAG CTT ACA AGC CCT GTT GTG GCA GAA AGT CCA AAA TTA AGT CAA TTT CTC GAA TGT TCG GGA CAA CAC CGT CTT TCA GGT TTT Asn Ser Val Lys Glu Leu Thr Ser Pro Val Val Ala Glu Ser Pro Lys> 630 AAA CCT TAA TTT GGA ATT

FIGURE 12 (2 of 2)

PCT/US94/12352

WO 95/12676

OspC-K48 Sequence Range: 1 to 630 22/133

		. 1	LO	•		20			30			4	10		
	•		•	•		•		•	•		•		•	•	
ATG	AAA	AAG	TAA	ACA	TTA	AGT	GCG	ATA	TTA	ATG	ACT	ATT	TTT	TTA	TTT
				TGT											
Met	Lys	Lys	Asn	Thr	Leu	Ser	Ala	Ile	Leu	Met	Thr	Leu	Phe	Leu	Phe>
E 0			60				70			80			90		
50 •		•	*		•	•	•	•		*		•	•		•
ATA	TCT	TGT	AAT	AAT	TCA	GGT	GGG	GAT	ACC	GCA	TCT	ACT	AAT	CCT	GAT
				TTA											
Ile	Ser	Cys	Asn	Asn	Ser	Gly	Gly	Asp	Thr	Ala	Ser	Thr	Asn	Pro	Asp>
10	טנ		-	110			120		•	13	•		•	140	
GAG	- -	CCA	444	GGA	CT	דממ	لبلت	ACA	СТА	ልጥል	»GC	444	222	ארד א	ACA
				CCT											
															Thr>
•	•														
	150			16	50		3	170			180			19	90
•	*		•		•	*	~~	•		•	~~~	~~~	•		•
				TTT AAA											
															Ile>
									-3 -						
	:	200			210			22	20		2	230			240
•		•		•	•		•		•	•		•		•	•
	TCT	* ATA		• GAA	ctt			ААА	• GCT		GGT	AAA			CAT
AGT	TCT AGA	± ATA TAT	CTA	CTT	CTT GAA	CGA	TTA	AAA TTT	GCT CGA	TAA	GGT CCA	AAA TTT	CAT	TAT	CAT GTA
AGT	TCT AGA	± ATA TAT	CTA	CTT	CTT GAA	CGA	TTA	AAA TTT	GCT CGA	TAA	GGT CCA	AAA TTT	CAT	TAT	CAT
AGT	TCT AGA	ATA TAT Ile	CTA	CTT	CTT GAA Leu	CGA	TTA	AAA TTT	GCT CGA	TAA	GGT CCA	AAA TTT	CAT Val	TAT	CAT GTA
AGT Ser	TCT AGA Ser	ATA TAT Ile	CTA Asp	CTT Glu	CTT GAA Leu	CGA Ala 260	TTA Asn	AAA TTT Lys	GCT CGA Ala 270	TAA Ile	GGT CCA Gly	AAA TTT Lys 28	CAT Val	TAT Ile	CAT GTA His>
AGT Ser CAA	TCT AGA Ser	ATA TAT Ile 2:	CTA Asp 50 GGT	CTT Glu * TTA	CTT GAA Leu	CGA Ala 260 GCT	TTA Asn AAT	AAA TTT Lys • GCG	GCT CGA Ala 270 GGT	TAA Ile CAA	GGT CCA Gly	AAA TTT Lys 28	CAT Val 0	TAT Ile	CAT GTA His>
AGT Ser CAA GTT	TCT AGA Ser • AAT TTA	ATA TAT Ile 2: AAT TTA	CTA Asp 50 GGT CCA	CTT Glu TTA AAT	CTT GAA Leu AAT TTA	CGA Ala 260 GCT CGA	TTA Asn AAT TTA	AAA TTT Lys • GCG CGC	GCT CGA Ala 270 GGT CCA	TAA Ile CAA GTT	GGT CCA Gly AAC TTG	AAA TTT Lys 28 GGA CCT	CAT Val 0 TCA AGT	TAT Ile TTG AAC	CAT GTA His>
AGT Ser CAA GTT	TCT AGA Ser • AAT TTA	ATA TAT Ile 2: AAT TTA	CTA Asp 50 GGT CCA	CTT Glu TTA AAT	CTT GAA Leu AAT TTA	CGA Ala 260 GCT CGA	TTA Asn AAT TTA	AAA TTT Lys • GCG CGC	GCT CGA Ala 270 GGT CCA	TAA Ile CAA GTT	GGT CCA Gly AAC TTG	AAA TTT Lys 28 GGA CCT	CAT Val 0 TCA AGT	TAT Ile TTG AAC	CAT GTA His>
AGT Ser CAA GTT	TCT AGA Ser • AAT TTA	ATA TAT Ile 2: AAT TTA	CTA Asp 50 GGT CCA	CTT Glu TTA AAT	CTT GAA Leu AAT TTA	CGA Ala 260 GCT CGA Ala	TTA Asn AAT TTA	AAA TTT Lys • GCG CGC	GCT CGA Ala 270 GGT CCA Gly	TAA Ile CAA GTT	GGT CCA Gly AAC TTG	AAA TTT Lys 28 GGA CCT	CAT Val 0 TCA AGT	TAT Ile TTG AAC	CAT GTA His>
AGT Ser CAA GTT Gln	TCT AGA Ser • AAT TTA	ATA TAT Ile 2: AAT TTA	CTA Asp 50 GGT CCA Gly	CTT Glu TTA AAT	CTT GAA Leu AAT TTA	CGA Ala 260 GCT CGA Ala	TTA Asn AAT TTA Asn	AAA TTT Lys • GCG CGC	GCT CGA Ala 270 GGT CCA Gly	TAA Ile CAA GTT Gln	GGT CCA Gly AAC TTG	AAA TTT Lys 28 GGA CCT	CAT Val 30 • TCA AGT Ser	TAT Ile TTG AAC	CAT GTA His>
AGT Ser CAA GTT Gln 290	TCT AGA Ser AAT TTA Asn	ATA TAT Ile 2: AAT TTA Asn	CTA Asp 50 GGT CCA Gly 300 TAT	CTT Glu TTA AAT Leu	CTT GAA Leu AAT TTA Asn	CGA Ala 260 GCT CGA Ala 31	AAT TTA ASN  O ACC	AAA TTT Lys GCG CGC Ala	GCT CGA Ala 270 GGT CCA Gly	CAA GTT Gln 320 ACA	GGT CCA Gly AAC TTG Asn	AAA TTT Lys 28 GGA CCT Gly	CAT Val 30 TCA AGT Ser 330	TAT Ile TTG AAC Leu	CAT GTA His> TTA AAT Leu>
CAA GTT Gln 290 GCA CGT	TCT AGA Ser AAT TTA ASD	ATA TAT Ile 2: AAT TTA Asn	CTA Asp 50 GGT CCA Gly 300 TAT ATA	CTT Glu TTA AAT Leu GCA CGT	CTT GAA Leu AAT TTA ASD	CGA Ala 260 GCT CGA Ala 3: TCA	AAT TTA ASD ACC TGG	AAA TTT Lys GCG CGC Ala CTA GAT	GCT CGA Ala 270 GGT CCA Gly ATA TAT	CAA GTT Gln 320 ACA	GGT CCA Gly AAC TTG ASI GAA CTT	AAA TTT Lys 28 GGA CCT Gly AAA TTT	CAT Val 30 TCA AGT Ser 330 TTA AAT	TAT Ile TTG AAC Leu AGT TCA	CAT GTA His> TTA AAT Leu> AAA TTT
CAA GTT Gln 290 GCA CGT	TCT AGA Ser AAT TTA ASD	ATA TAT Ile 2: AAT TTA Asn	CTA Asp 50 GGT CCA Gly 300 TAT ATA	CTT Glu TTA AAT Leu GCA CGT	CTT GAA Leu AAT TTA ASD	CGA Ala 260 GCT CGA Ala 3: TCA	AAT TTA ASD ACC TGG	AAA TTT Lys GCG CGC Ala CTA GAT	GCT CGA Ala 270 GGT CCA Gly ATA TAT	CAA GTT Gln 320 ACA	GGT CCA Gly AAC TTG ASI GAA CTT	AAA TTT Lys 28 GGA CCT Gly AAA TTT	CAT Val 30 TCA AGT Ser 330 TTA AAT	TAT Ile TTG AAC Leu AGT TCA	CAT GTA His> TTA AAT Leu>
CAA GTT Gln 290 GCA CGT Ala	TCT AGA Ser AAT TTA ASD	ATA TAT Ile 2: AAT TTA Asn	CTA ASP 50 GGT CCA Gly 300 TAT ATA Tyr	CTT Glu TTA AAT Leu GCA CGT	CTT GAA Leu AAT TTA ASD	CGA Ala 260 GCT CGA Ala 3: TCA	AAT TTA ASD ACC TGG	AAA TTT Lys GCG CGC Ala CTA GAT	GCT CGA Ala 270 GGT CCA Gly ATA TAT	CAA GTT Gln 320 ACA TGT	GGT CCA Gly AAC TTG Asn GAA CTT Glu	AAA TTT Lys 28 GGA CCT Gly AAA TTT	CAT Val 30 TCA AGT Ser 330 TTA AAT Leu	TAT Ile TTG AAC Leu AGT TCA Ser	CAT GTA His> TTA AAT Leu> AAA TTT
CAA GTT Gln 290 GCA CGT Ala	TCT AGA Ser AAT TTA ASD GGA CCT Gly	ATA TAT Ile 2: AAT TTA Asn	CTA ASP 50 GGT CCA Gly 300 TAT ATA Tyr	CTT Glu TTA AAT Leu GCA CGT Ala	CTT GAA Leu AAT TTA ASD	CGA Ala 260 GCT CGA Ala 3: TCA	AAT TTA ASD 10 ACC TGG Thr	AAA TTT Lys GCG CGC Ala CTA GAT	GCT CGA Ala 270 GGT CCA Gly ATA TAT	CAA GTT Gln 320 ACA TGT	GGT CCA Gly AAC TTG ASI GAA CTT	AAA TTT Lys 28 GGA CCT Gly AAA TTT	CAT Val 30 TCA AGT Ser 330 TTA AAT Leu	TAT Ile TTG AAC Leu AGT TCA	CAT GTA His> TTA AAT Leu> AAA TTT
CAA GTT Gln 290 GCA CGT Ala 3	TCT AGA Ser AAT TTA Asn CCT Gly	ATA TAT Ile 2: AAT TTA Asn GCC CGG Ala	CTA ASP 50 GGT CCA Gly 300 TAT ATA Tyr	CTT Glu TTA AAT Leu GCA CGT Ala	CTT GAA Leu AAT TTA ASN ATA TAT Ile	CGA Ala 260 GCT CGA Ala 3: TCA AGT Ser	AAT TTA ASN 10 . ACC TGG Thr 360 . AAT	AAA TTT Lys GCG CGC Ala CTA GAT Leu	GCT CGA Ala 270 GGT CCA Gly ATA TAT Ile	CAA GTT Gln 320 ACA TGT Thr	GGT CCA Gly AAC TTG Asn GAA CTT Glu	AAA TTT Lys 28 GGA CCT Gly AAA TTT Lys	CAT Val  80 TCA AGT Ser  330 TTA AAT Leu  GCT	TAT Ile  TTG AAC Leu  AGT TCA Ser  B80 AAG	CAT GTA His> TTA AAT Leu> AAA TTT Lys> AAC
CAA GTT Gln 290 GCA CGT Ala 3	TCT AGA Ser AAT TTA Asn CGA CCT Gly AAA TTT	ATA TAT Ile 2: AAT TTA Asn GCC CGG Ala AAT	CTA Asp 50 CCA Gly 300 TAT ATA Tyr TCA AGT	CTT Glu TTA AAT Leu GCA CGT Ala 350	CTT GAA Leu AAT TTA Asn ATA TAT Ile	CGA Ala 260 GCT CGA Ala 33 TCA AGT Ser	AAT TTA ASD TGG Thr 360 AAT TTA	AAA TTT Lys GCG CGC Ala CTA GAT Leu	GCT CGA Ala 270 GGT CCA Gly ATA TAT Ile	CAA GTT Gln 320 ACA TGT Thr	GGT CCA Gly * AAC TTG ASD CTT Glu 70 * GAA CTT	AAA TTT Lys 28 GGA CCT Gly AAA TTT Lys GAG CTC	CAT Val  TCA AGT Ser  TTA AAT Leu  GCT CGA	TAT Ile  TTG AAC Leu  AGT TCA Ser AAG TTCA	CAT GTA His> TTA AAT Leu> AAA TTT Lys> AAC

OspC-K48

420 400 410 390 CAT TCT GAA GCA TTT ACT AAT AGA CTA AAA GGT TCT CAT GCA CAA CTT GTA AGA CTT CGT AAA TGA TTA TCT GAT TTT CCA AGA GTA CGT GTT GAA His Ser Glu Ala Phe Thr Asn Arg Leu Lys Gly Ser His Ala Gln Leu> 460 470 480 440 GGA GTT GCT GCT ACT GAT GAT CAT GCA AAA GAA GCT ATT TTA AAG CCT CAA CGA CGA CGA TGA CTA CTA GTA CGT TTT CTT CGA TAA AAT TTC Gly Val Ala Ala Ala Thr Asp Asp His Ala Lys Glu Ala Ile Leu Lys> 490 500 510 520 TCA AAT CCT ACT AAA GAT AAG GGT GCT AAA GCA CTT AAA GAC TTA TCT AGT TTA GGA TGA TTT CTA TTC CCA CGA TTT CGT GAA TTT CTG AAT AGA Ser Asn Pro Thr Lys Asp Lys Gly Ala Lys Ala Leu Lys Asp Leu Ser> 550 560 570 530 540 GAA TCA GTA GAA AGC TTG GCA AAA GCA GCG CAA GAA GCA TTA GCT AAT CTT AGT CAT CTT TCG AAC CGT TTT CGT CGC GTT CTT CGT AAT CGA TTA Glu Ser Val Glu Ser Leu Ala Lys Ala Ala Gln Glu Ala Leu Ala Asn> 580 590 600 610 620 TCA GTT AAA GAA CTT ACA AAT CCT GTT GTG GCA GAA AGT CCA AAA AAA AGT CAA TTT CTT GAA TGT TTA GGA CAA CAC CGT CTT TCA GGT TTT TTT Ser Val Lys Glu Leu Thr Asn Pro Val Val Ala Glu Ser Pro Lys Lys> CCT TAA GGA ATT Pro \*\*\*>

FIGURE 13 (2 of 2)

PCT/US94/12352

24/133

OspC-PKO Sequence Range: 1 to 639

30 40 20 ATG AAA AAG AAT ACA TTA AGT GCG ATA TTA ATG ACT TTA TTT TTA TTT TAC TTT TTC TTA TGT AAT TCA CGC TAT AAT TAC TGA AAT AAA AAT AAA Met Lys Lys Asn Thr Leu Ser Ala Ile Leu Met Thr Leu Phe Leu Phe> 80 90 60 70 50 ATA TCT TGT AGT AAT TCA GGG AAA GGT GGG GAT TCT GCA TCT ACT AAT TAT AGA ACA TCA TTA AGT CCC TTT CCA CCC CTA AGA CGT AGA TGA TTA Ile Ser Cys Ser Asn Ser Gly Lys Gly Gly Asp Ser Ala Ser Thr Asn> 110 120 CCT GCT GAC GAG TCT GCG AAA GGG CCT AAT CTT ACA GAA ATA AGC AAA GGA CGA CTG CTC AGA CGC TTT CCC GGA TTA GAA TGT CTT TAT TCG TTT Pro Ala Asp Glu Ser Ala Lys Gly Pro Asn Leu Thr Glu Ile Ser Lys> 170 160 180 AAA ATT ACA GAT TCT AAT GCA TTT GTA CTT GCT GTT AAA GAA GTT GAG TTT TAA TGT CTA AGA TTA CGT AAA CAT GAA CGA CAA TTT CTT CAA CTC Lys Ile Thr Asp Ser Asn Ala Phe Val Leu Ala Val Lys Glu Val Glu> 220 230 240 200 210 ACT TTG GTT TTA TCT ATA GAT GAA CTT GCT AAG AAA GCT ATT GGT CAA TGA AAC CAA AAT AGA TAT CTA CTT GAA CGA TTC TTT CGA TAA CCA GTT Thr Leu Val Leu Ser Ile Asp Glu Leu Ala Lys Lys Ala Ile Gly Gln> 260 270 280 250 AAA ATA GAC AAT AAT AAT GGT TTA GCT GCT TTA AAT AAT CAG AAT GGA TTT TAT CTG TTA TTA TTA CCA AAT CGA CGA AAT TTA TTA GTC TTA CCT Lys Ile Asp Asn Asn Gly Leu Ala Ala Leu Asn Asn Gln Asn Gly> 290 300 310 320 330 TCG TTG TTA GCA GGA GCC TAT GCA ATA TCA ACC CTA ATA ACA GAA AAA AGC AAC AAT CGT CCT CGG ATA CGT TAT AGT TGG GAT TAT TGT CTT TTT Ser Leu Leu Ala Gly Ala Tyr Ala Ile Ser Thr Leu Ile Thr Glu Lys> 340 350 360 370 380 TTG AGT AAA TTG AAA AAT TTA GAA GAA TTA AAG ACA GAA ATT GCA AAG AAC TCA TTT AAC TTT TTA AAT CTT CTT AAT TTC TGT CTT TAA CGT TTC Leu Ser Lys Leu Lys Asn Leu Glu Glu Leu Lys Thr Glu Ile Ala Lys>

. OspC-PKO

Pro Lys Lys Pro \*\*\*>

420 410 400 390 GCT AAG AAA TGT TCC GAA GAA TTT ACT AAT AAA CTA AAA AGT GGT CAT CGA TTC TTT ACA AGG CTT CTT AAA TGA TTA TTT GAT TTT TCA CCA GTA Ala Lys Lys Cys Ser Glu Glu Phe Thr Asn Lys Leu Lys Ser Gly His> 470 450 440 GCA GAT CTT GGC AAA CAG GAT GCT ACC GAT GAT CAT GCA AAA GCA GCT CGT CTA GAA CCG TTT GTC CTA CGA TGG CTA CTA GTA CGT TTT CGT CGA Ala Asp Leu Gly Lys Gln Asp Ala Thr Asp Asp His Ala Lys Ala Ala> 520 500 490 ATT TTA AAA ACA CAT GCA ACT ACC GAT AAA GGT GCT AAA GAA TTT AAA TAA AAT TIT TGT GTA CGT TGA TGG CTA TIT CCA CGA TIT CIT AAA TIT Ile Leu Lys Thr His Ala Thr Thr Asp Lys Gly Ala Lys Glu Phe Lys> 560 570 550 540 530 GAT TTA TTT GAA TCA GTA GAA GGT TTG TTA AAA GCA GCT CAA GTA GCA CTA AAT AAA CTT AGT CAT CTT CCA AAC AAT TTT CGT CGA GTT CAT CGT Asp Leu Phe Glu Ser Val Glu Gly Leu Leu Lys Ala Ala Gln Val Ala> 620 610 600 590 580 CTA ACT AAT TCA GTT AAA GAA CTT ACA AGT CCT GTT GTA GCA GAA AGT GAT TGA TTA AGT CAA TTT CTT GAA TGT TCA GGA CAA CAT CGT CTT TCA Leu Thr Asn Ser Val Lys Glu Leu Thr Ser Pro Val Val Ala Glu Ser> 630 CCA AAA AAA CCT TAA GGT TTT TTT GGA ATT

PCT/US94/12352

26/133

OspC-TRO Sequence Range: 1 to 624

10 20 ATG AAA AAG AAT ACA TTA AGT GCG ATA TTA ATG ACT TTA TTT TTA TTT TAC TIT TIC TIA TGT AAT TCA CGC TAT AAT TAC TGA AAT AAA AAT AAA Met Lys Lys Asn Thr Leu Ser Ala Ile Leu Met Thr Leu Phe Leu Phe> 70 80 60 50 ATA TCT TGT AAT AAT TCA GGT GGG GAT TCT GCA TCT ACT AAT CCT GAT TAT AGA ACA TTA TTA AGT CCA CCC CTA AGA CGT AGA TGA TTA GGA CTA Ile Ser Cys Asn Asn Ser Gly Gly Asp Ser Ala Ser Thr Asn Pro Asp> 130 140 100 110 GAG TCT GCA AAA GGA CCT AAT CTT ACC GTA ATA AGC AAA AAA ATT ACA CTC AGA CGT TTT CCT GGA TTA GAA TGG CAT TAT TCG TTT TTT TAA TGT Glu Ser Ala Lys Gly Pro Asn Leu Thr Val Ile Ser Lys Lys Ile Thr> 180 150 160 190 GAT TCT AAT GCA TTT TTA CTG GCT GTG AAA GAA GTT GAG GCT TTG CTT CTA AGA TTA CGT AAA AAT GAC CGA CAC TTT CTT CAA CTC CGA AAC GAA Asp Ser Asn Ala Phe Leu Leu Ala Val Lys Glu Val Glu Ala Leu Leu> 220 230 . 240 TCA TCT ATA GAT GAA CTT TCT AAA GCT ATT GGT AAA AAA ATA AAA AAT AGT AGA TAT CTA CTT GAA AGA TTT CGA TAA CCA TTT TTT TAT TTT TTA Ser Ser Ile Asp Glu Leu Ser Lys Ala Ile Gly Lys Lys Ile Lys Asn> 270 260 250 GAT GGT ACT TTA GAT AAC GAA GCA AAT CGA AAC GAA TCA TTG ATA GCA CTA CCA TGA AAT CTA TTG CTT CGT TTA GCT TTG CTT AGT AAC TAT CGT Asp Gly Thr Leu Asp Asn Glu Ala Asn Arg Asn Glu Ser Leu Ile Ala> 300 310 320 330 290 GGA GCT TAT GAA ATA TCA AAA CTA ATA ACA CAA AAA TTA AGT GTA TTG CCT CGA ATA CTT TAT AGT TTT GAT TAT TGT GTT TTT AAT TCA CAT AAC Gly Ala Tyr Glu Ile Ser Lys Leu Ile Thr Gln Lys Leu Ser Val Leu> 350 360 370 380 AAT TCA GAA GAA TTA AAG AAA AAA ATT AAA GAG GCT AAG GAT TGT TCC TTA AGT CTT CTT AAT TTC TTT TTT TAA TTT CTC CGA TTC CTA ACA AGG

Asn Ser Glu Glu Leu Lys Lys Lys Ile Lys Glu Ala Lys Asp Cys Ser>

OSPC-TRO

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CTT TTT AA	r ACI	WC7 v		CAT	JATAL POLITICAL	CTA	TCA	GTA	CGT	CTC	GAA	CCA	TAT
Glu Lys Ph	A TGA	IGA I	110	on.	Tuc	yen.	Sar	His	Ala	Glu	Leu	Gly	Ile>
Glu Lys Ph	e Thr	rnr i	Lys	Leu	ւրչ	vah	JC1						
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440		. •	450			•	*	•		•		•	•
• •		•			-			C C TT	እሞፐ	dade y		ACA	CAT
CAA AGC GT	T CAG	GAT (	GAT	AAT	GCA	AAA	AAA	CCI	WII	111	WALL VAVA	<b>₩</b>	CTA
GTT TCG CA	A GTC	CTA (	CTA	TTA	CGT	TTT	777	CGA	TAA	AA1	111	101	Ui a
Gln Ser Va	1 Gln	Asp A	Asp	Asn	Ala	Lys	Lys	Ala	He	Leu	Lys	inr	H12>
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GGA ACT AF	A GAC	AAG	GGT	GCT	AAA	GAA	CTT	GAA	GAG	TTA	TTT	AAA	TCA
00m max m	AL CAC	TITLE (	CCA	CGA	TTT	CTT	GAA	CTT	CTC	AAT	AAA	1.1.1	AGT
Gly Thr Ly	c Aen	INS	Glv	Ala	Lvs	Glu	Leu	Glu	Glu	Leu	Phe	Lys	Ser>
GIA III D	3 NOP	270			-						-		
c20	540			5	50			560			570		
530	J40		•	_	*	•		•		•	. •		•
CTA GAA A	- mm-	ጥር እ	222	GCA	GCG	CAA	GCA	GCA	TTA	ACT	AAT	TCA	GTT
GAT CTT TO	, 110	104	WAL.	CCT	CCC	GTT	CGT	CGT	TAA	TGA	ATT	AGT	CAA
Leu Glu S	.G AAC	VQ1	T 11.0	Ala	Ala	Gln	Ala	Ala	Leu	Thr	Asn	Ser	Val>
Leu Glu S	er Leu	Ser	гуз	YIG	AIG	01							
					600			6	10			620	
580		590		_	500			•	4			•	
•	•				-		CAA			N N N		CCI	427
AAA GAG C	IT ACA	AAT	CCT	GTT	GIG	GCA	GAA	, wo				CCI	አጥጥ
TIT CIC G	AA TGT	TTA	GGA	CAA	CAC	CGT	CIT	TCA	i GGI	111	111	GUA Dec	. WII
Lys Glu L	eu Thr	Asn	Pro	Val	Val	. Ala	Glu	sei	Pro	Lys	Lys	PIC	>

WO 95/12676 PCT/US94/12352

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P93

Sequence Range: 1 to 2102

10 20 30 40

ATG AAA AAA ATG TTA CTA ATC TTT AGT TTT TTT CTT ATT TTC TTG AAT TAC TTT TTT TAC AAT GAT TAG AAA TCA AAA AAA GAA TAA AAG AAC TTA Met Lys Lys Met Leu Leu Ile Phe Ser Phe Phe Leu Ile Phe Leu Asn>

50 60 70 80 90

GGA TTT CCT GTT AGT GCA AGA GAA GTT GAT AGG GAA AAA TTA AAG GAC CCT AAA GGA CAA TCA CGT TCT CTT CAA CTA TGG-CTT TTT AAT TTC CTG Gly Phe Pro Val Ser Ala Arg Glu Val Asp Arg Glu Lys Leu Lys Asp>

100 110 120 130 140

TTT GTT AAT ATG GAT CTT GAG TTT GTA AAT TAT AAA GGC CCT TAT GAT AAA CAA TTA TAC CTA GAA CTC : A CAT TTA ATA TTT CCG GGA ATA CTA Phe Val Asn Met Asp Leu Glu Phe Val Asn Tyr Lys Gly Pro Tyr Asp>

150 160 170 180 190

TCT ACA AAT ACA TAT GAA CAA ATA GTG GGT ATT GGG GAG TTT TTA GCA AGA TGT TTA TGT ATA CTT GTT TAT CAC CCA TAA CCC CTC AAA AAT CGT Ser Thr Asn Thr Tyr Glu Gln Ile Val Gly Ile Gly Glu Phe Leu Ala>

200 210 220 230 240

AGA CCG TTG ACC AAT TCC AAT AGC AAC TCA AGT TAT TAT GGT AAA TAT TCT GGC AAC TGG TTA AGG TTA TCG TTG AGT TCA ATA ATA CCA TTT ATA ATG Pro Leu Thr Asn Ser Asn Ser Asn Ser Ser Tyr Tyr Gly Lys Tyr>

250 260 270 280

TTT ATT AAT AGA TTT ATT GAT GAT CAA GAT AAA AAA GCA AGC GTT GAT AAA TAA TTA TCT AAA TAA CTA CTA GTT CTA TTT TTT CGT TCG CAA CTA Phe Ile Asn Arg Phe Ile Asp Asp Gln Asp Lys Lys Ala Ser Val Asp>

290 300 310 320 330

GTT TTT TCT ATT GGT AGT AAG TCA GAG CTT GAC AGT ATA TTG AAT TTA CAA AAA AGA TAA CCA TCA TTC AGT CTC GAA CTG TCA TAT AAC TTA AAT Val Phe Ser Ile Gly Ser Lys Ser Glu Leu Asp Ser Ile Leu Asn Leu>

340 350 360 370 380

AGA AGA ATT CTT ACA GGG TAT TTA ATA AAG TCT TTC GAT TAT GAC AGG TCT TCT TAA GAA TGT CCC ATA AAT TAT TTC AGA AAG CTA ATA CTG TCC Arg Arg Ile Leu Thr Gly Tyr Leu Ile Lys Ser Phe Asp Tyr Asp Arg>

FIGURE 16 (1 of 5)

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 	. Cm	CC1	C	~~~						•			•		•
101	WOI	CCT	CAA	114	ATT	CC1.	AAG	GIT	ATT	ACA	ATA	TAT	TAA	GCT	GTT
AGA	104	COI	CII	AAI	TAA	CGA	110	CAA	TAA	TGT	TAT	ATA	TTA	CGA	CAA
Ser	ser	Ala	GIU	reu	116	ATS	rys	vaı	11e	Thr	lle	Tyr	Asn	Ala	Val>
		440			450										
_	•	140	•	. •	450		_	40	50	_	•	670			480
<b>.</b>		-	~~~	-	-	~~~								•	•
TAT	AGA	GGA	CAI	116	GAT	TAT	TAT	AAA	GGG	TTT	TAT	ATT	GAG	GCT	GCT
ATA	TCT	CCT	CIA	AAC	CIA	ATA	ATA	TTT	CCC	AAA	ATA	TAA	CTC	CGA	CGA
Tyr	Arg	GIA	ASP	ren	Asp	lyr	lyr	rys	GIÀ	Phe	Tyr	Ile	Glu	Ala	Ala>
			90						<b>530</b>						•
		4:	•		•	500			510	<b>==</b> • •	٠.	52	20		
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777	AAG	101	777	AC.	ጥጥጥ	CITT	WAI	CCT	CCI	CIT	TCT	AGG	GTT	TAT	agt
LAN	TTC	Cor	VVI	1CV	111	Clu	114	212	Cla	GAA	AGA	TCC	CAA	ATA	TCA
ren	Lys	361	reu	Ser	Lys	GIU	ASII	Ala	GIA	ren	Ser	Arg	Val	Tyr	Ser>
530			540			55	in.			660			F7.0		
-		•	J40		•	٦.	•	•	-	•			570		_
CAG	TGG	GCT	GGA	AAG	ACA	CAA	ATA	عملت	<b>ት</b> ፖፕ	CCT	حت	25.2	N.C	C 3 T	
GTC	ACC	CGA	CCT	TTC	TGT	GTT	TAT	222	711	CCI	C23	4.4.4.	70	CAL	Air
Gln	Trp	Ala	Glv	Lvs	Thr	Gln	Ile	Phe	Tle	Pro	ten	111	Tue	CIM	Ile>
			,	_, _						•••		by 3	Lys	MSD	i.e>
58	30		9	590			600			61	0		,	520	
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TTG	TCT	GGA	AAT	ATT	GAG	TCT	GAC	ATT	GAT	ATT	GAC	AGT	T-1	CTT	202
AAC	AGA	CCT	TTA	TAA	CTC	AGA	CTG	TAA	CTA	TAA	CTG	TCA	AAT	CAA	TCT
Leu	Ser	Gly	Asn	Ile	Glu	Ser	Asp	Ile	Asp	Ile	CZÁ	Ser	Leu	Val	Thr>
							_		•		•			•	
	630			64	10		•	550			660			67	70
•	•		•		•	•		•		•	•		•		•
GAT	AAG	CTC	GTG	GCA	GCT	CTT	TTA	AGT	CAA	3 3 7	GAA	400	~~~		AAC
CTA		010							GAA	w			GG	CTT.	TTG
	TTC	CAC	CAC	CGT	CGA	GAA	AAT	TCA	CTT	TTA	CTT	CGT	CCA	CAA	
Asp	TTC	CAC	CAC	CGT	CGA	GAA	AAT	TCA	CTT	TTA	CTT	CGT	CCA	CAA	Asn>
Asp	TTC Lys	CAC Val	CAC	CGT	Ala	GAA	AAT	TCA Ser	CTT Glu	TTA	CTT	CGT	CCA	CAA	Asn>
Asp	TTC Lys	CAC	CAC	CGT	CGA	GAA	AAT	TCA	CTT Glu	TTA	CTT Glu	CGT	CCA	CAA	Asn>
Asp •	TTC Lys	CAC Val	CAC Val	CGT Ala	CGA Ala 690	GAA Leu	AAT Leu	TCA Ser	CTT Glu	TTA Asn	CTT Glu	CGT Ala	CCA Gly	CAA Val	Asn>
Asp • TTT	TTC Lys GCA	CAC Val 80	CAC Val	CGT Ala • ATT	CGA Ala 690 *	GAA Leu GAT	AAT Leu	TCA Ser 7(	Glu  GGC	TTA Asn	CTT Glu 7	CGT Ala 110 CAT	CCA Gly AAG	CAA Val •	Asn>
Asp • TTT AAA	TTC Lys GCA CGT	CAC Val 80 AGA TCT	CAC Val GAT CTA	CGT Ala * ATT TAA	CGA Ala 690 ACA TGT	GAA Leu GAT CTA	AAT Leu ATT TAA	TCA Ser 7( CAA GTT	Glu Glu GGC CCG	TTA Asn GAA CTT	CTT Glu ACT TGA	CGT Ala 10 CAT GTA	CCA Gly AAG TTC	CAA Val • GCA CGT	Asn> 721 GAT CTA
Asp • TTT AAA	TTC Lys GCA CGT	CAC Val 80 AGA TCT	CAC Val GAT CTA	CGT Ala * ATT TAA	CGA Ala 690 ACA TGT	GAA Leu GAT CTA	AAT Leu ATT TAA	TCA Ser 7( CAA GTT	Glu Glu GGC CCG	TTA Asn GAA CTT	CTT Glu ACT TGA	CGT Ala 10 CAT GTA	CCA Gly AAG TTC	CAA Val • GCA CGT	Asn>
Asp • TTT AAA	TTC Lys GCA CGT	CAC Val 80 AGA TCT Arg	CAC Val GAT CTA Asp	CGT Ala * ATT TAA	CGA Ala 690 * ACA TGT Thr	GAA Leu GAT CTA Asp	AAT Leu ATT TAA	TCA Ser 7( CAA GTT	Glu  O  GGC  CCG  Gly	TTA Asn GAA CTT	CTT Glu ACT TGA	CGT Ala 710 • CAT GTA His	CCA Gly AAG TTC Lys	CAA Val • GCA CGT	Asn> 721 GAT CTA
Asp • TTT AAA	TTC Lys GCA CGT	CAC Val 80 AGA TCT Arg	CAC Val GAT CTA	CGT Ala * ATT TAA	CGA Ala 690 * ACA TGT Thr	GAA Leu GAT CTA	AAT Leu ATT TAA	TCA Ser 7( CAA GTT	Glu Glu GGC CCG	TTA Asn GAA CTT	CTT Glu ACT TGA	CGT Ala 10 CAT GTA	CCA Gly AAG TTC Lys	CAA Val • GCA CGT	Asn> 721 GAT CTA
TTT AAA Phe	GCA CGT Ala	CAC Val 880 AGA TCT Arg	CAC Val GAT CTA Asp	CGT Ala * ATT TAA Ile	CGA Ala 690 * ACA TGT Thr	GAA Leu GAT CTA Asp	AAT Leu • ATT TAA Ile	TCA Ser 7( CAA GTT Gln	GGC GGC GGC GGC G1y	Asn GAA CTT Glu	CTT Glu ACT TGA Thr	CGT Ala 710 CAT GTA His	CCA Gly AAG TTC Lys	CAA Val • GCA CGT Ala	Asn> 721 GAT CTA Asp>
ASP TIT AAA Phe	GCA CGT Ala	CAC Val 80 AGA TCT Arg	GAT CTA Asp	CGT Ala * ATT TAA Ile GAT	CGA Ala 690 ACA TGT Thr	GAA Leu GAT CTA Asp	AAT Leu ATT TAA Ile	TCA Ser 70 CAA GTT Gln • GAC	GGC CCG Gly	ASN GAA CTT Glu	CTT Glu ACT TGA Thr	CGT Ala 710 CAT GTA His 76	CCA Gly AAG TTC Lys	CAA Val GCA CGT Ala	Asn> 723 GAT CTA Asp>
TTT AAA Phe CAA GTT	CCA CGT Ala GAT CTA	CAC Val 80 AGA TCT Arg 7: AAA TTT	GAT CTA Asp	CGT Ala ATT TAA Ile GAT CTA	CGA Ala 690 ACA TGT Thr ATT TAA	GAA Leu GAT CTA Asp 40 • GAA CTT	AAT Leu ATT TAA Ile TTA AAT	TCA Ser 70 CAA GTT Gln GAC CTG	GGC CCG Gly 750 AAT TTA	ATT TAA	CTT Glu ACT TGA Thr CAT GTA	CGT Ala 710 CAT GTA His 76 GAA CTT	CCA Gly AAG TTC Lys 50 AGT TCA	CAA Val • GCA CGT Ala • GAT CTA	Asn> 721 GAT CTA Asp> TCC AGG
TTT AAA Phe CAA GTT	CCA CGT Ala GAT CTA	CAC Val 80 AGA TCT Arg 7: AAA TTT	GAT CTA Asp	CGT Ala ATT TAA Ile GAT CTA	CGA Ala 690 ACA TGT Thr ATT TAA	GAA Leu GAT CTA Asp 40 • GAA CTT	AAT Leu ATT TAA Ile TTA AAT	TCA Ser 70 CAA GTT Gln GAC CTG	GGC CCG Gly 750 AAT TTA	ATT TAA	CTT Glu ACT TGA Thr CAT GTA	CGT Ala 710 CAT GTA His 76 GAA CTT	CCA Gly AAG TTC Lys 50 AGT TCA	CAA Val • GCA CGT Ala • GAT CTA	Asn> 723 GAT CTA Asp>
TTT AAA Phe CAA GTT	CCA CGT Ala GAT CTA	CAC Val 80 AGA TCT Arg 7: AAA TTT	GAT CTA Asp	CGT Ala ATT TAA Ile GAT CTA	CGA Ala 690 ACA TGT Thr ATT TAA	GAA Leu GAT CTA Asp GAA CTT Glu	AAT Leu ATT TAA Ile TTA AAT	TCA Ser 70 CAA GTT Gln GAC CTG	GGC CCG Gly 750 AAT TTA Asn	TTA Asn GAA CTT Glu ATT TAA Ile	CTT Glu ACT TGA Thr CAT GTA	CGT Ala 710 CAT GTA His 76 GAA CTT	AAG TTC Lys 60 AGT TCA Ser	CAA Val • GCA CGT Ala • GAT CTA	Asn> 721 GAT CTA Asp> TCC AGG
TITT AAA Phe  CAA GTT Gln	CCA CGT Ala GAT CTA	CAC Val 80 AGA TCT Arg 7: AAA TTT	GAT CTA Asp ATT TAA Ile	CGT Ala ATT TAA Ile GAT CTA	CGA Ala 690 ACA TGT Thr ATT TAA	GAA Leu GAT CTA Asp GAA CTT Glu	AAT Leu ATT TAA Ile TTA AAT Leu	TCA Ser 70 CAA GTT Gln GAC CTG	GGC CCG Gly 750 AAT TTA Asn	ATT TAA	CTT Glu ACT TGA Thr CAT GTA	CGT Ala 710 CAT GTA His 76 GAA CTT	CCA Gly AAG TTC Lys 50 AGT TCA	CAA Val • GCA CGT Ala • GAT CTA	Asn> 721 GAT CTA Asp> TCC AGG
ASP TITT AAA Phe CAA GTT Gln 770	GCA CGT Ala GAT CTA Asp	CAC Val 80 AGA TCT Arg 7: AAA TTT Lys	GAT CTA ASP ATT TAA Ile 780	ATT TAA Ile GAT CTA ASP	CGA Ala 690 * ACA TGT Thr ATT TAA Ile	GAA Leu GAT CTA Asp GAA CTT Glu	AAT Leu ATT TAA Ile TTA AAT Leu	TCA Ser 70 CAA GTT Gln GAC CTG Asp	GGC CCG Gly 750 AAT TTA Asn	GAA CTT Glu ATT TAA Ile	ACT TGA Thr CAT GTA His	CGT Ala 710 CAT GTA His 76 GAA CTT Glu	AAG TTC Lys 60 AGT TCA Ser 810	CAA Val GCA CGT Ala GAT CTA Asp	Asn> 721 GAT CTA Asp> TCC AGG Ser>
ASP TITT AAA Phe CAA GTT Gln 770 AAT	GCA CGT Ala GAT CTA Asp	CAC Val 80 AGA TCT Arg 7: AAA TTT Lys	GAT CTA ASP ATT TAA Ile 780	CGT Ala ATT TAA Ile GAT CTA ASP	CGA Ala 690 * ACA TGT Thr ATT TAA Ile	GAA Leu GAT CTA Asp 40 • GAA CTT Glu 79	AAT Leu  ATT TAA Ile  TTA AAT Leu  90  AAT	TCA Ser 7( CAA GTT Gln GAC CTG Asp	CTT Glu  00  GGC CCG Gly  750  AAT TTA ASD	GAA CTT Glu ATT TAA Ile	CTT Glu ACT TGA Thr CAT GTA His	CGT Ala 710 CAT GTA His 76 GAA CTT Glu CTT	AAG TTC Lys 60 AGT TCA Ser 810	CAA Val GCA CGT Ala GAT CTA Asp	Asn> 723 GAT CTA Asp> TCC AGG Ser>
ASP  TITT AAA Phe  CAA GTT Gln  770 AAT TTA	GCA CGT Ala GAT CTA Asp	CAC Val 80 AGA TCT Arg 7: AAA TTT Lys	GAT CTA ASP ATT TAA Ile 780 GAA CTT	CGT Ala * ATT TAA Ile GAT CTA ASP	CGA Ala 690 ACA TGT Thr ATT TAA Ile ATT TAA	GAA Leu GAT CTA Asp GAA CTT Glu 79 GAA CTT	AAT Leu  ATT TAA Ile  TTA AAT Leu  AAT TTA	TCA Ser 70 CAA GTT Gln GAC CTG Asp	CTT Glu  00  GGC CCG Gly  750  AAT TTA Asn  AGG TCC	GAA CTT Glu ATT TAA Ile	CTT Glu ACT TGA Thr CAT GTA His	CGT Ala  110  CAT GTA His  76  GAA CTT Glu  CTT GAA	AAG TTC Lys 60 * AGT TCA Ser 810 GAA CTT	CAA Val GCA CGT Ala GAT CTA ASP	Asn> 723 GAT CTA Asp> TCC AGG Ser>

8	20			830			840			8	50			860	
ACA	CAT	GAA	GAG	CAT	AAA	-	GAG	ATT	C:A	АСТ	CyC.	•	CIT	•	AAA
TGT	СТА	CTT	CTC	GTA	TTT	TTT	CTC	TAA	CII	TCA	GTC	CAA	CTA	CGA	TTT
Thr	Asp	Glu	Glu	His	Lys	Lys	Glu	Ile	Glu	Ser	Gln	Val	Asp	Ala	Lys>
	870			8:	80		·	890			900			•	• •
•	•		•	•	•	•	`	•		•	300		•	9	10
AAG	AAA	CAA	AAG	GAA	GAG	CTA	GAT	AAA	AAG	GCA	ATA	AAT	CTT	GAT	444
TTC	TTT	GTT	TTC	CTT	CTC	GAT	CTA	TTT	TTC	CGT	TAT	TTA	GAA	CTA	TTT
Lys	Lys	Gln	Lys	Glu	Glu	Leu	Asp	Lys	Lys	Ala	Ile	Asn	Leu	Asp	Lys>
		920			930			0,	10			) E A			
•	•	•		•	*		•	٠.	• _		3	950			960
GCT	CAG	CAA	AAA	TTA	GAT	TCT	GCT	GAA	GAT	AAT	TTA	GAT	GTT	C2.3	2G2
CGA	GTC	GTT	TTT	AAT	CTA	AGA	CGA	CTT	CTA	TTA	AAT	CTA	CAA	GTT	TCT
Ala	Gln	Gln	Lys	Leu	Asp	Ser	Ala	Glu	Asp	Asn	Leu	Asp	Val	Gln	Arg>
		91	70		9	80			990			100	าก		-
	•		•	•		•		•	•		•		•	•	
TAA	ACT	GTT	AGA	GAG	AAA	TTA	CAA	GAG	GAT	TTA	AAC	GAA	ATT	AAC	AAG
TTA	TGA	CAA	TCT	CTC	TTT	TAA	GTT	CTC	CTA	TAA	TTG	CTT	TAA	TTG	TTC
Asn	Thr	Val	Arg	Glu	Lys	Ile	Gln	Glu	Asp	Ile	Asn	Glu	Ile	Asn	Lys>
1010		:	1020			103	30		10	040		1	L050		
•		•	•		•		• .	•		•		•	•		•
GAA	AAG	AAT	TTA	CCA	AAG	CCT	GGT	GAT	GTA	AGT	TCT	CCT	AAA	GTT	GAT
CTT	TTC	TTA	AAT	GGT	TTC	GGA	CCA	CTA	CAT	TCA	AGA	GGA	TIT	CAA	CTA
GIA	Lys	ASD	Leu	Pro	Lys	Pro	Gly	Asp	Val	Ser	Ser	Pro	Lys	Val	Asp>
100	50		10	70		3	1080			109	0		11	.00	
	•	•		•		•	•		•		•	•		•	
AAG	CAA	CTA	CAA	ATA	AAA	GAG	AGC	CTG	GAA	GAT	TTG	CAG	GAG	CAG	CTT
TTC	GTT	GAT	GTT	TAT	TTT	CTC	TCG	GAC	CTT	CTA	AAC	GTC	CTC	GTC	GAA
Lys	GIN	Leu	Gin	116	Lys	Glu	Ser	Leu	Glu	Asp	Leu	Gln	Glu	Gln	Leu>
	1110		_	112	20		11	30		1	140			115	0
444	GAA	ልርተ	CCT	CAT	CAA	እእጥ	CNC		101	•	•		•		•
TTT	CTT	TCA	CCA	CTA	CTT	TT A	CAG	TTT	AGA TCT	GAA	ATT	GAA	AAG	CAA	ATT
Lys	Glu	Thr	Gly	Asp	Glu	Asn	Gln	Lvs	Ara	Glu	Tle	Glu	TYC	GIT	TAA Ile>
		•	_	•				•				010	<i>D</i> <sub>3</sub> 3	<b>G1</b> 11	1167
	11	160		. 1	170			118	30	_	11	90		1	200
GAA	ATC	AAA	AAA	AGT	GAT	GAA	244	CTT	מדים	444	እርጥ	*	C 3 M	•	•
CTT	TAG	TTT	TTT	TCA	CTA	CTT	TTC	GAA	TAA	4444 4444	AG I	777	CTA	GAT	AAA TTT
Glu	Ile	Lys	Lys	Ser	Asp	Glu	Lys	Leu	Leu	Lys	Ser	Lvs	Asp	ASD	Lys>
										-		•		·	-,
	•	12:	•		12	220		•	1230			124	10		
GCA	AGT	AAA	GAT	GGT	444	פכר	TTC	- CAT	<del>Стт</del>	Chm	CC	C	T-00	•	mc~
CGT	TCA	TTT	CTA	CCA	TTT	CGG	AAC	CTA	440	CTA	COA	CTT	TTA	AAT	TCT
Ala	Ser	Lys	Asp	Gly	Lys	Ala	Leu	ask	Leu	Asp	Aro	G) u	Leu	TED	AGA Ser>
		-	-	-	-						9		-cu	W211	

FIGURE 16 (3 of 5)

1280 1270 1250 1260 AAA GCT TCT AGC AAA GAA AAA AGT AAA GCC AAG GAA GAA ATA ACC TTT CGA AGA TCG TTT CTT TTT TCA TTT CGG TTC CTT CTT TAT TGG Lys Ala Ser Ser Lys Glu Lys Ser Lys Ala Lys Glu Glu Glu Ile Thr> 1340 1330 1320 1310 1300 AAG GGT AAG TCA CAG AAA AGC TTA GGC GAT TTG AAT AAT GAT GAA AAT TTC CCA TTC AGT GTC TTT TCG AAT CCG CTA AAC TTA TTA CTA CTT TTA Lys Gly Lys Ser Gln Lys Ser Leu Gly Asp Leu Asn Asn Asp Glu Asn> 1370 . ----1380 1360 1350 CTT ATG ATG CCA GAA GAT CAA AAA TTA CCT GAG GTT AAA AAA TTA GAT GAA TAC TAC GGT CTT CTA GTT TTT AAT GGA CTC CAA TTT TTT AAT CTA Leu Met Met Pro Glu Asp Gln Lys Leu Pro Glu Val Lys Lys Leu Asp> 1430 1420 1410 1400 AGC AAA AAA GAA TTT AAA CCT GTT TCT GAG GTT GAG AAA TTA GAT AAG TCG TTT TTT CTT AAA TTT GGA CAA AGA CTC CAA CTC TTT AAT CTA TTC Ser Lys Lys Glu Phe Lys Pro Val Ser Glu Val Glu Lys Leu Asp Lys> 1480 1470 1460 1450 ATT TTC AAG TCT AAT AAC AAT GTT GGA GAA TTA TCA CCG TTA GAT AAA TAA AAG TTC AGA TTA TTG TTA CAA CCT CTT AAT AGT GGC AAT CTA TTT Ile Phe Lys Ser Asn Asn Asn Val Gly Glu Leu Ser Pro Leu Asp Lys> 1520 1530 1510 1500 1490 TCT TCT TAT ANA GAC ATT GAT TCA ANA GAG GAG ACA GTT ANT ANA GAT AGA AGA ATA TTT CTG TAA CTA AGT TTT CTC CTC TGT CAA TTA TTT CTA Ser Ser Tyr Lys Asp Ile Asp Ser Lys Glu Glu Thr Val Asn Lys Asp> 1570 1560 1550 GTT AAT TTG CAA AAG ACT AAG CCT CAG GTT AAA GAC CAA GTT ACT TCT CAA TTA AAC GTT TTC TGA TTC GGA GTC CAA TTT CTG GTT CAA TGA AGA Val Asn Leu Gln Lys Thr Lys Pro Gln Val Lys Asp Gln Val Thr Ser> 1620 1610 1600 1590 TTG AAT GAA GAT TTG ACT ACT ATG TCT ATA GAT TCC AGT AGT CCT GTA AAC TTA CTT CTA AAC TGA TGA TAC AGA TAT CTA AGG TCA TCA GGA CAT . Leu Asn Glu Asp Leu Thr Thr Met Ser Ile Asp Ser Ser Ser Pro Val> 1670 1660 1650 1640 TTT TTA GAG GTT ATT GAT CCA ATT ACA AAT TTA GGA ACT CTT CAA CTT AAA AAT CTC CAA TAA CTA GGT TAA TGT TTA AAT CCT TGA GAA GTT GAA Phe Leu Glu Val Ile Asp Pro Ile Thr Asn Leu Gly Thr Leu Gln Leu>

1720 1700 1690 ATT GAT TTA AAT ACT GGT GTT AGG CTT AAA GAA AGC ACT CAG CAA GGC TAA CTA AAT TTA TGA CCA CAA TCC GAA TTT CTT TCG TGA GTC GTT CCG Ile Asp Leu Asn Thr Gly Val Arg Leu Lys Glu Ser Thr Gln Gln Gly> 1770 1760 1750 1740 1730 ATT CAG CGG TAT GGA ATT TAT GAA CGT GAA AAA GAT TTG GTT GTT ATT TAA GTC GCC ATA CCT TAA ATA CTT GCA CTT TTT CTA AAC CAA CAA TAA Ile Gln Arg Tyr Gly Ile Tyr Glu Arg Glu Lys Asp Leu Val Val Ile> 1820 1800 1790 1780 AAA ATG GAT TCA GGA AAA GCT AAG CTT CAG ATA CTT GAT AAA CTT GAA TTT TAC CTA AGT CCT TTT CGA TTC GAA GTC TAT GAA CTA TTT GAA CTT Lys Met Asp Ser Gly Lys Ala Lys Leu Gln Ile Leu Asp Lys Leu Glu> 1850 1860 1840 1830 AAT TTA AAA GTG GTA TCA GAG TCT AAT TTT GAG ATT AAT AAA AAT TCA TTA AAT TTT CAC CAT AGT CTC AGA TTA AAA CTC TAA TTA TTT TTA AGT Asn Leu Lys Val Val Ser Glu Ser Asn Phe Glu Ile Asn Lys Asn Ser> 1910 1900 1890 1880 TCT CTT TAT GTT GAT TCT AAA ATG ATT TTA GTA GCT GTT AGG GAT AAA AGA GAA ATA CAA CTA AGA TTT TAC TAA AAT CAT CGA CAA TCC CTA TTT Ser Leu Tyr Val Asp Ser Lys Met Ile Leu Val Ala Val Arg Asp Lys> 1960 1950 1940 1930 GAT AGT AGT AAT GAT TGG AGA TTG GCC AAA TTT TCT CCT AAA AAT TTA CTA TCA TCA TTA CTA ACC TCT AAC CGG TTT AAA AGA GGA TTT TTA AAT Asp Ser Ser Asn Asp Trp Arg Leu Ala Lys Phe Ser Pro Lys Asn Leu> 2000 1990 1980 1970 GAT GAG TTT ATT CTT TCA GAG AAT AAA ATT ATG CCT TTT ACT AGC TTT CTA CTC AAA TAA GAA AGT CTC TTA TTT TAA TAC GGA AAA TGA TCG AAA Asp Glu Phe Ile Leu Ser Glu Asn Lys Ile Met Pro Phe Thr Ser Phe> 2060 2050 2040 2030 TCT GTG AGA AAA AAT TTT ATT TAT TTG CAA GAT GAG TTT AAA AGT CTA AGA CAC TCT TTT TTA AAA TAA ATA AAC GTT CTA CTC AAA TTT TCA GAT Ser Val Arg Lys Asn Phe Ile Tyr Leu Gln Asp Glu Phe Lys Ser Leu> 2100 2080 2090 2070

GTT ATT TTA GAT GTA AAT ACT TTA AAA AAA GTT AAG TA CAA TAA AAT CTA CAT TTA TGA AAT TTT TTT CAA TTC AT Val Ile Leu Asp Val Asn Thr Leu Lys Lys Val Lys Xxx>

FIGURE 16 (5 of 5)

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1	TAAAAAAAT	TGTTACTAAT	CTTTAGTTTT	TITCITATIT	CTTTGAATGG	ATTTCCTCTT
61	አስማምር አስርርርር	AACTTGATAA	GGAAAAATTA	AAGGATTTTG	TTAATATGGA	TCTTGAGTTT
121	מדמד אמ מדים	AAGGTCCTTA	TGATTCTACA	AATACATATG	AAÇAAATAGT	AGSTATTGGT
121	CACHALALAYC	CAAGACCATT	GATTAATTCC	AATAGCAACT	CAATTTATTA	TGGTAAATAT
2/1	ATLATTRATTT	GATTTATTGA	TGATCAAGAT	AAAAAAGCAA	GCGTTGATGT	TTTTTCTATT
301	CCTACTACCT	CACAGCTTGA	CAGTATATTG	AATCTAAGAA	GAATTCTTAC	AGGGTATTTG
361	עדור אנים ע ע עדע ע	TTGATTATGA	AAGATCTAGT	GCTGAATTAA	TTGCTAAGGT	TATTACAATA
421	CATABATCOTTS	TTTATAGAGG	<b>GGATTTAAAT</b>	TATTATAAAG	AGGTTTATAT	TGAGGCTGCT
401	עבור אוים עי עיובע	TAACTAAAGA	AAATGCAGGT	CTTTCTAGAG	TGTACAGTCA	ATGGGCTGGA
5/1	AACACACAAA	TATTTATTCC	TCTTAAAAAG	TATTTTATA	CTGGAAAAGT	TGAGTCTGAC
601	STALEMENTA	ACAGTTTGGT	TACAGATAAG	GTTGTGGCAG	-ETETTTTAAG	CGAGAATGAA
661	CCACCTCTTA	ACTITICCAAG	AGATATTACA	GATATTCAAG	GCGAAACTCA	TAAAGCAGAT
721	CARCATARAR	TIGATATIGA	ATTAGATAAT	GTTCATAAAA	<b>GTGATTCCAA</b>	TATAACAGAG
721	ACTATTCAGA	ATTTAAGAGA	TCAGCTTGAA	AAGGCTACAG	ATGAAGAGCA	TAGAAAAGAG
841	ATTGAAAGTC	AGGTTGATGC	TAAAAAGAAA	CAAAAAGAAG	AACTAGATAA	AAAGGCAATC
907	CATCTTCATA	AAGCCCAACA	AAAATTAGAT	TCTTCTGAAG	ATAATTTAGA	TATTCAAAGG
961	GATACTGTTA	GAGAGAAGAT	TCAAGAGGAT	ATTGACGAGA	TTAATAAAGA	AAAGAATTTG
1021	CCAAAACCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AGCTACAAAT	AAAAGAGAGT
1081	CTAGAAGACT	TGCAGGAACA	<b>GCTTAAAGAA</b>	ACTAGCGATG	AAAATCAAAA	AAGAGAAATT
1141	GAAAAGCAAA	TTGAAATCAA	AAAAAGTGAT	GAAGAACTTT	TAAAAAGTAA	AGATCCTAAA
1201	GCATTAGATC	TTAATGGAGA	TTTAAATTCT	AAAGTTTCTA	GTAAAGAAAA	AATTAAAGGC
1261	AAAGAAGGAG	AAATAGTCAA	AGAGGAATCA	AAGGCAAGTT	TAGCTGATTT	GAATAATGAC
1321	GAAAATCTTA	TGAGGCCGGA	AGATCAAAAA	TTATCTGAGG	TTAAAAAATT	AGATAGTAAA
1381	AAAAATTTAA	AACCIGITIC	TGAGATTGAG	AGAGTAAATG	AAATTTCGAA	GTCTAACAAC
1441	AATGAGATTA	GTGAATCATC	ACCATTATAT	AAGCCTTCTT	ATAGCGATAT	GGATTCAAAA
1501	GAGGGTATAG	ATAATAAAGA	TGTTAACTTG	CAAGAAACCA	AGTCTCAAAC	TAAAAGTCAA
1561	CCTACTTCTT	TAAATCAAGA	TTTGACTACI	· ATGTCTATAG	ATTCTAGTAA	TCCTGTATTT
1621	TTAGAGGTTA	TTGATCCTAT	TACAAATTTA	GGAACGCTTC	AACITATTGA	TTTGAATACC
1681	GGTGTTAGAC	TTAAAGAAAC	TACTCAGCAA	GCATTCAGC	GGTATGGAAT	TTATGAACGT
1741	GAAAAAGATT	TAGTICITAT	`TAAAATGGAT	TCAGGAAAAG	CCAAGCTTCA	AATACTTAAT
1801	AAACTTGAGA	L ATTTAAAAGT	CATATCGGAC	TCTAATTTTC	AGATTAATAA	AAATTCATCT
1861	CTTTATGTTC	ACTCTAAAAT	GATTTTAGTA	GTTGTGAGAG	ATAGTGGTAA	TGTTTGGAGA
1921	TTGGCTAAAT	TTTCTCCTA	CAKATTTAAA 1	GAGTTTATTC	TITCAGAGAA	TAAAATTTTG
1981	CCTTTTACTA	GCTTTTCTGT	GAGAAAGAA?	TTATTTATTT 1	TGCAGGATGA	GTTTAAAAGT
2041	CTTATTACTI	TAGATGTAA	A TACTTTAAAJ	A AAAGTTAAGI	A	

p93 - BO

	•					
1	ATGAAAAAA	TGTTACTAAT	CTTTAGTTTT	TITCITGITT	TTTTAAATGG	ATTTCCTCTT
61	AATGCAAGGG	AAGTTGATAA	GGAAAAATTA	AAGGACTTTG	TTAATATGGA	TCTTGAATTT
121	GTTAATTACA	AGGGTCCTTA	TGATTCTACA	GATACATATG	AACAAATAGT	AGGTATTGGG
181	<b>GAGTTTTTAG</b>	CAAGGCCGTT	GAACAATTCC	AATAGTAATT	CAAGTTATTA	TGGTAAATAT
241	TTTGTTAATA	GATTTATTGA	CGATCAAGAT	AAAAAAGCAA	GTGTTGATAT	TTTTTCTATT
301	GGTAGTAAGT	CAGAGCTTGA	TAGTATATTA	AATCTAAGAA	GAATTCTTAC	AGGGTATTTA
361	ATGAAGICTT	TTGATTATGA	GAGGTCTAGT	GCGGAATTAA	TŢGCTAAAGC	TATTACAATA
421	TATAATGCTG	TTTATAGAGG	AGATTTAGAT	TATTACAAAG	AGTTTTATAT	TGAGGCTTCT
				CTTTCTAGGG		
541	AAGACACAAA	TATTTATTCC	TCTTAAAAAG	TATTTTATAA	CTGGAAATGT	TGAGTCTGAC
				<b>GTGGTGGÇAG</b>		
661	TCAGGTGTTA	ACTITICAAG	<b>AGATATTACA</b>	GACATTCAAG	GCGAAACTCA	TAAAGCAGAT
				TTTCATGAAA		
				AAAGCTACAG		
				CAAAAGGAAG		
				TTTGCTGAAG		
				ATTAACGAGA		
				GTTGATAAGC		
				GCTAGTGATG		
				GAAGAACTTT		
				AAAGCTTCTA		
				AAAAATTTAG		
				AATGAGGTTA		
				GAGGGTGTAG		
				CCTACTTCGT		
				TTAGAGGTTA		
		•		GGTGTTAGAC		
				GAAAAAGATT		
				AAACTCGAGA		
				CTTTATGTTG		
		•		TIGGCTAAAT		
				CCTTTTACTA		
			ACTTAAAAGC	TTAGTTACTT	TAGATGTAAA	TACTTTAAAA
1981	AAAGTTAAGT	A				

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1	ATGAAAAAA	TGTTACTAAT	CTTTAGTTTT	TTTCTTATTT	CTTTGAATGG	ATTTCCCCTT
61	AATGCAAGGG	AAGTTGATAA	<b>GGAAAAATTA</b>	<b>AAGGACTTTG</b>	TTAATATGGA	TCTTGAGTTT
121	GTAAACTATA	AAGGTCCTTA	TGATTCTACA	AATACATATG	<b>AACAAATAGT</b>	AGGTATTGGT
181	GAGTTTTTAG	CAAGACCATT	GATTAATTTC	AATAGCAACT	CAAGTTATTA	TGGTAAATAT
241	TTTATTAATA	GATTTATTGA	CGATCAAGAT	AAAAAAGCAA	GCGTTGATGT	TTTTTCTATT
301	AGTAGTAAGT	CACAGCTTGA	CAGTATATTG	AATTTAAGAA	GAATTCTTAC	AGGGTATTTG
361	ATAAAGTCTT	TTGATTATGA	<b>AAGATCTAGT</b>	<b>GCTGAATTAA</b>	TTGCCAAGGT	TATTACAATA
421	CATAATGCTG	TTTATAGAGG	TGATTTAAAT	TATTATAAAG	AGTTTTATAT	TGAGTCTGCT
481	TTAAAGTCTT	TAACTAAAGA	AAATGCAGGT	CTTTCTAGAG	TGTACAGTCA	ATGGGCTGGA
541	AAGACACAAA	TATTTATTCC	TCTTAAAAAG	AATATTTTAT	CTGGAAAAAT	TGAGTCTGAC
	ATTGATATTG					
	GCAGGTGTTA					
721	CAAGATAAAA	TTGATATTGA	ATTAGATAAT	GTTCATGAAA	GTGATTCCAA	TATAACAGAA
781	ACTATTGAGA	ATTTAAGAGA	TCAGCTTGAA	AAGGCTACAG	ATGAAGAGCA	TAGAAAAGAG
841	ATTGAAAGTC	AAGTTGATGC	TAAAAAGAAA	CAAAAAGAAG	<b>AACTAGATAA</b>	AAAGGCAATC
901	GATCTTGATA	AAGCCCAACA	AAAATTAGAT	TTTTCTGAAG	ATAATTTAGA	TATTCAAAGG
961	GATACTGTTA	GAGAGAAGAT	TCAAGAGGAT	ATTAACGAGA	TTAATAAGGA	AAAGAATTTA
1021	CCAAAACCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AGCTACAAAT	AAAAGAGAGT
1081	CTAGAAGACT	TGCAGGAGCA	GCTTAAAGAA	ACTAGCGATG	AAAATCAAAA	AAGAGAAATT
1141	GAAAAGCAAA	TTGAAATCAA	AAAAAGTGAT	GAAGAACTTT	TAAAAAGCAA	AGATCCTAAA
1201	GCATTAGATC	TTAATCGAGA	TTTAAATTCT	AAAGCTTCTA	GTAAAGAAAA	AATTAAAGGC
1261	AAAGAAAAAG	AAATAGTCAA	AGAGAAATCA	AAGGTAAGTT	TAGGTGATTT	GGATAATGAC
1321	GAAACCCTTA	TGACGCCGGA	AGATCAAAAA	TTATCTGAGG	TTAAAAAATT	AGATAGTAAA
1381	<b>AATTTAA</b>	AACCTGTTTC	TGAGATTGAG	AGAGTAAATG	AAATTTCAAA	GTCTAACAAC
1441	AATGAGGTTA	GCAAATCATC	ACCATTAGAT	AAGCCTTCTT	ATAGTGATAT	CGATTCAAAA
1501	GAGGTTGTAG	ATAATAAAGA	TGTTAATTTG	CAAGAAACCA	AGCCTCAAGC	TAAAAGTCAA
1561	TCTACTTCTT	TAAATCAAGA	TTTGATTACT	ATGTCTATAG	ATTCTAGTAA	TCCTGTATTT
1621	TTAGAGGTTA	TTGATCCTAT	TACAAATTTA	GGAATGCTTC	AACTTATTGA	TTTAAATACT
1681	GGTGTTAGAC	TTAAAGAAAG	CACTCAGCAA	GGCATTCAGC	GTTATGGAAT	TTATGAACGT
1741	GAAAAAGATT	TAGTTGTTAT	TAAAATGGAT	TCAGGAAAAG	CTAAGCTTCA	AATACTTAAT
1801	AAACTTGAGA	ATTTAAAAGT	GATATCAGAG	TCTAATTTTG	AGATTAATAA	AAATTCATCT
1861	CTTTATGTTG	ACTCTAAAAT	GATTTTAGTA	GCTGTGAAAG	ATAGTGGTAA	TGTTTGGAGA
1921	TTGGCTAAAT	TTTCTCCTAA	AAATTTAGAT	GAGTTTATTC	TTTCAGAGAA	TAAAATTTTG
1981	CCTTTTACTA	GCTTTTCTGT	GAGAAAGAAT	TTTATTTATT	TGCAAGATGA	GTTTAAAAGT
2041	CTTATTACTT	TAGATGTAAA	TACTTTAAAA	AAAGTTAAGT	A	

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1	ATGAAAAAA	TGTTACTAAT	CTTTAGTTTT	TITCITGITI	TTTTAAATGG	ATTTCCTCTT
61	DODAGOOMAA	AAGTTGATAA	GGAAAAATTA	AAGGACTTTG	TTAATATGGA	TCTTGAATTT
121	CTTAATTACA	AGGGTCCTTA	TGATTCTACA	AATACATATG	AACAAATAGT	AGGTATTGGG
181	CACHITITIAG	CAAGGCCGTT	GATCAATTCC	AATAGTAATT	CAAGTTATTA	TGGTAAATAT
241	ATAATTOTTT	GATTTATTGA	CGATCAAGAT	AAAAAAGCAA	GTGTTGATAT	TITITCTATT
301	GGTAGTAAGT	CAGAGCTTGA	TAGTATATTA	AATCTAAGAA	GAATTCTTAC	AGGGTATITA
361	ATGAAGTCTT	TTGATTATGA	GAGGTCTAGT	GCGGAATTAA	TTGCTAAAGC	TATTACAATA
421	TATAATGCTG	TTTATAGAGG	AGATTTAGAT	TATTACAAAG	AGTTTTATAT	TGAGGCTTCT
481	TTGAAGTCTT	TGACTAAAGA	AAATGCAGGT	CTTTCTAGGG	TGTACAGTCA	ATGGGCTGGG
541	AAGACACAAA	TATTTATTCC	TCTTAAAAAG	TATTTTTAT	CTGGAAATGT	TGAGTCTGAC
601	ATTGATATTG	ATAGTTTGGT	TACAGATAAG	GTGGTGGCAG	CTCTTTTAAG	TGAGAATGAA
661	TCAGGTGTTA	ACTITICAAG	<b>AGATATTACA</b>	GACATTCAAG	GCGAAACTCA	TAAAGCAGAT
721	CAAGATAAAA	TTGATATTGA	ATTAGATAAT	ATTCATGAAA	GTGATTCCAA	TATAACAGAA
781	ACTATTGAGA	ATTTAAGGGA	TCAGCTTGAA	AAAGCTACAG	ATGAAGAGCA	TAAAAAAGAG
841	ATTGAAAGTC	AGGTTGATGC	TAAAAAGAAA	CAAAAGGAAG	AATTAGATAA	AAAGGCAATT
901	GATCTTGATA	AAGCTCAACA	AAAATTAGAT	TTTGCTGAAG	ATAATCTAGA	TATTCAAAGG
961	GATACTGTTA	GAGAGAAGCT	TCAAGAGAAT	ATTAACGAGA	CTAATAAGGA	AAAGAATTTA
1021	CCAAAGCCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AACTACAAAT	AAAAGAGAGC
1081	CTGGAAGATT	TGCAGGAGCA	<b>GCTTAAAGAA</b>	ACTGGTGATG	AAAATCAGAA	AAGAGAAATT
1141	GAAAAGCAAA	TTGAAATCAA	AAAAAGTGAT	GAAAAGCTTT	TAAAAAGTAA	AGATGATAAA
1201	GCAAGTAAAG	ATGGTAAAGC	CTTGGATCTT	GATCGAGAAT	TAAATTCTAA	AGCTICTAGC
1261	AAAGAAAAA	GTAAAGCCAA	GGAAGAAGAA	ATAACCAAGG	GTAAGTCACA	GAAAAGCTTA
1321	GGCGATTTGA	ATAATGATGA	AAATCTTATG	ATGCCAGAAG	ATCAAAAATT	ACCTGAGGTT
1381	AAAAAATTAG	ATAGCAAAAA	AGAATTTAAA	CCTGTTTCTG	AGGTTGAGAA	attagataag
1441	ATTITCAAGT	CTAATAACAA	TGTTGGAGAA	TTATCACCGT	TAGATAAATC	TTCTTATAAA
1501	GACATTGATT	CAAAAGAGGA	GACAGTTAAT	AAAGATGTTA	ATTTGCAAAA	GACTAAGCCT
1561	CAGGTTAAAG	ACCAAGTTAC	TTCTTTGAAT	GAAGATTTGA	CTACTATGTC	TATAGATTCC
		TATTTTTAGA				
1681	ATTGATTTAA	ATACTGGTGT	TAGGCTTAAA	GAAAGCACTC	AGCAAGGCAT	TCAGCGGTAT
1741		AACGTGAAAA				
1801		TTGATAAACT				
1861	TTAAAAATA	CATCTCTTTA	TGTTGATTCT	AAAATGATTT	TAGTAGCTGT	TAGGGATAAA
1921	GATAGTAGTA	ATGATTGGAG	ATTGGCCAAA	TTTTCTCCTA	<b>AAAATTTAGA</b>	TGAGTTTATT
1981		TATTAAAATA				
2041	TTGCAAGATC	AGTITAAAAG	TCTAGTTATT	TTAGATGTAA	. ATACTTTAAA	AAAAGTTAAG
2101	TAAAGCC					

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1	ATGAAAAAAA	TGTTACTAAT	CTTTAGTTTT	TTTCTTGTTT	TTTTAAATGG	ATTTCCTCTT
	2200022000	A ACTIVED TO A	CCDDDDTTA	AAGGACTTIG	TIMAIAIGGA	TOTTOWNITT
7 7 7	COMPARATE A	VICTUALLY A	TYPATACA	AATACATATG	WACWANINGI	MOGINIIOOG
181	C & COMMONDAR & C	CA PICTURE AT	CATTAATTCC	AATAGTAATI	CAAGITATTA	1001WWWIWI
243	WILLY VILLE AND VILLE	COUNTRAINT A	CCATCAAGAT	AAAAAAGCAA	GIGITGATAT	TITITICIATI
201	CCTACTAACT	CACACCTTCA	TACTATATTA	AATCTAAGAA	GAATICITAC	AGGGTATTTA
263	PULL P V CARCALAI	A SYPATYPASYTYP	GAGGTCTAGT	GCGGAATTAA	TIGCTAAAGC	TATTACAATA
422	WALLY VALCALCE	SOASATATT	AGATTTAGAT	TATTACAAAG	AGITITATAT	TGAGGCTTCT
401	TALANCO V CANAM	TCACTAAAGA	AAATGCAGGT	CTTTCTAGGG	TGTACAGTCA	ATGGGCTGGG
E 47	4447474744	J. Markatakan	TCTTAAAAAG	AATATTTTAT	CIGGAAAIGI	TGAGICIGAC
601	Nucleon Warred	Published Cal	TACAGATAAG	GTGGTGGCAG	CICITITAAG	TGAGAATGAA
661	WAS CONCURS.	<b>ACTALACT BY</b>	AGATATTACA	GACATICAAG	GCGAAACTCA	TAAAGCAGAT .
721	CAACATAAAA	TTTCATATYTCA	ATTAGATAAT	TTTCATGAAA	GIGATICCAA	TATAACAGAA
701	A CALVALATAC D C.D.	ATTENDACECA	TCAGCTTGAA	AAAGCTACAG	ATGAAGAGCA	TAAAAAAGAG
0/1	ATTICADACTIC	ACCTITICATION	TAAAAAGAAA	CAAAAGGAAG	AATTAGATAA	AAAGGCAATT
001	CAUCALLANCY A	ADGCTYCAACA	AAAATTAGAT	TTTGCTGAAG	ATAATCTAGA	TATICAAAGG
961	מישיביער מישיבי	CACACAAGCT	TKAAGAAAAT	ATTAACGAGA	CTAATAAGGA	AAAGAATITA
1021	CCDDDCCCTC	CTCATCTAAG	TTCTCCTAAG	GTTGATAAGC	AGTTGCAGAT	AAAAGAGAGT
1001	CTACAACATT	TYCEARGAGEA	CCTTAAAGAA	GCTAGTGATG	AAAATCAAAA	AAGAGAAATA
1141	CANADCCAAA	TTCAAATCAA	AAAAAATGAT	GAAGAACTTT	TTAAAAATAA	AGATCATAAA
1201	CCATTACATC	TTARGCARGA	ATTAAATTCT	AAAGCTTCTA	GTAAAGAAAA	AATTGAAGGC
1261	CARCARCAGG	ATABACAATT	AGATAGTAAA	AAAAATTTAG	AGCCTGTTTC	TGAGGCTGAT
1221	ADACTACATA	AAATTTCCAA	GTCTAACAAC	: AATGAGGTTA	GTAAATTATC	CCCGTTAGAT
1201	CACCUTATOTATE	ATACCGACAT	TGATTCGAAA	. GAGGGTGTAG	ATAACAAAGA	TGTTGATTTG
1441	ATT A A A A A A A A	AACCCCAAGT	TGAAAGTCAA	CCTACTTCGT	' TAAATGAAGA	CTTGATTGAT
1501	CACACADADAC	ልጥፕሃዮጵሮፕልል	TCCTGTCTT	· TTAGAGGTTA	. TCGATCCGAT	TACAAATTTA
1561	CCAACCCTTC	AACTTATTGA	TTTGAATACC	GGTGTTAGAC	: TTAAAGAAAG	TGCTCAACAA
1621	CCTATTY ACC	GATATGGAAT	TTATGAACGI	`GAAAAAGATI	' TGGTTGTTAT	TAAAATAGAT
1681	TCAGGAAAAG	CTAAGCTTCA	GATACTIGAT	· AAACTCGAGA	ATTTAAAAGT	GATATCAGAG
1741	TCTAATTTTG	AGATTAATAA	AAATTCATCT	CTTTATGTTC	ACTOTAGAAT	GATTTTAGTA
1801	GTTGTTAAGG	ACGATAGTA	L TGCTTGGAGA	A TTGGCTAAAT	TTTCTCCTAA	AAATTTAGAT
1861	GAATTTATTC	TGTCAGAAA	TAAAATTTY	CCTTTTACTA	GCTTTGCTGT	GAGAAAGAAT
1921	TTTATTTATT	TGCAAGATG	ACTTAAAAG(	TTAGTTACT	TAGATGTAAA	TACTITAAAA
	AAAGTTAAGT					•

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_		TGTTACTAAT	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	TTTATTTY	TTTTGAATGG	ATTTCCTCTT
1	ATGAAAAAA	AAGTTGATAA	CITIAGITIT	AACCATTTTG	TTAATATGGA	TCTTGAGTTT
61	AATGCAAGGA	AAGTIGATAA AAGGTCCTTA	GGAAAAA11A	ANTACCTATG	AACAAATAGT	GGGTATTGGG
121	GTAAATTATA	CAAGACCGCT	TGATICTACA	AMINCOINTO	CAACTTATTA	TGGCAAATAT
181	GAGTTTTTAG	CAAGACCGCT	GACCAATICC	MAINOCARCI	CHALLCALCL	TTTTTCTATA
241	TTTATTAATA	GATTTATTGA	TGATCAAGAT	AMMONOCON	רבידישריים	ACCOTATATA
301	AGCAGCAAAT	CAGAGCTTGA	CAGTATATIG	WILLIAMON!	TYPETARGET	TATTACAATA
361	ATAAAGTCTT	TCGATTATGA	CAGGTCTAGT	GCAGANTIAN	CCLALANOOI	TCACCTTCCT
421	TATAATGCTG	TTTATAGAGG	AGATTIGGAT	TATTATAMO	ALLY COLLEGE	CACCCACCA
481	TTGAAGTCTT	TAACTAAAGA	AAACGCAGGT	CITICIAGG	TITACAGICA	OLOGOCIOGE
541	AAGACTCAAA	TATTTATTCC	TCTTAAAAAG	GATATTTIGT	CIGGWWINI	CARROTTE
601	ATTGATATTG	ACAGTTTGGT	TACAGATAAG	GTGATAGCAG	CICITITANG	COMMUNICAN
661	GCAGGCGTTA	ACTITGCAAG	AGATATTACA	GATATICAAG	GCGAAACTCA	TAAGGCAGAI
721	CAAGATAAGA	TTGATACTGA	ATTAGACAAT	ATCCATGAAA	GCGATTCTAA	TATAACAGAA
201	Z CALMANCA Z Z	PATALY PCCCY	TCAGCTTGAA	AAAGCTACAG	AIGAAGAGCA	TAAAAAGAG
043	AMMONATOR	<b>PECALICPACE</b>	ТАААААСААА	.GAAAAGGAAG	AGCTAGATAA	AAAGGCAATC
001	A DAY TATE OF A	AACCTCACCA	AAAATTAGAC	TCTGCTGAAG	ATAATITAGA	TGTTCAAAGA
061	CAMPCACALD	CACACAAAAT	TCAAGAGGAT	ATTAATGAGA	TTAATAAGGA	AAAGAATTIG
7021	CCANANCCTC	CTYCATYTTAAG	TTCTCCTAAA	GTTGATAAGC	AACTGCAAAT	AAAAGAGAGT
1001	CTACAACATT	TYCENCENCEN	GCTTAAAGAA	GCTGGTGATG	AAAANCAGAA	AAGAGAAATT
1141	CACAACCAAA	TTGAAATCAA	AAAAAGGGAC	GAAGAACTTT	TAAAAAGTAA	AGATGGCAAA
1201	CTABCTABAC	COAGTETTA	ATTAGATCTT	GATCGAGAAT	TATCCAAAGC	TICIAGIAAA
1261	CANADAGTA	ACCTUANCEN	AGAAGAAATA	ACTAAAGGTA	AATCACGGGC	AAGCTTAGGC
1321	CATTTCAATA	AAKAATAATA	CCTTATGTTG	CCAGAAGATC	AAAAATTACC	TGAAGATAAA
1201	እእስጥፕርርስጥል	CTABATTAGA	TGGTAAAAAA	GAATTTAAAC	CAGITICIGA	GGTTGAAAAA
1441	ТТАСАТААСА	TTTCCAAGTC	TAATAACAAT	GAGGTTGGCA	AGTTATCACC	ATTAGATAAG
1501	COTTOTATA	ATGATATTGA	TTCAAAAGAG	GAGGTAGATA	. ATAAAGCTAT	TAATTIGCAA
1561	AAGATCGACC	CTAAAGTTAA	AGACCAAACT	ACTICTIGA	. ATGAAGATTT	GGATAAAGAT
1621	מיייאמייאמייא	TYCTYTATAGA	TTCCAGCAGT	CCTGTATTTC	TAGAGGTTAT	TGATCCTATT
1681	ACAAATTTAG	CAACCCTGCA	GCTTATTGAT	` TTAAATACTG	GGGTTAGGCT	TAAGGAAAGC
1741	ACTUACUANC	CCATTCAGCG	GTATGGAATI	' TATGAACGTG	AAAAAGATTT	GGTTGTTATT
1 201	TRACETTAGE	CAGGAAAGGC	TAAGCTTCAA	<b>ATACTTAATA</b>	. AGCTTGAAAA	TTTGAAAGIG
1861	CTATYAGAGT	CTRAPTETTGA	GATCAATAAA	L AATTCATCTC	: TTTATGTTGA	CICTAAAATG
1021	ATTITICACAC	CTCTTAGAGA	TAAGGATGAT	· AGCAATGCTT	' GGAGATIGGC	TAAATITICI
1001	ייים ממממיים	TECATEACTT	TATTCTTTC	GAGAATAAAA	TTTTGCCTTT	TACTAGCTTT
2041	. CC1WWwy11	רבידידינבננ	TTATTTCCA	GATGAGCTTA	AAAATCTAGT	TATTTTAGAT
2101	101010000	TAAAAAAAT	מדמממי י			
210	r GIWWYIWCI I	TANAMANA	AMOIN			

### K48 OSP A/ PGAU OSP A FUSION

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	10					20			30 40						
	•		•	•		•		•	•		•		•	•	
ATG	AAA	AAA	TAT	TTA	TTG	GGA	ATA	GGT	CTA	ATA	TTA	GCC	TTA	ATA	GCA
TAC	TTT	TTT	ATA	AAT	AAC	CCT	TAT	CCA	GAT	TAT	AAT	CGG	AAT	TAT	CGT
Met	Lys	Lys	Tyr	Leu	Leu	Gly	Ile	Gly	Leu	Ile	Leu	Ala	Leu	Ile	Ala>
50			60				70			80			90		
		•	•		•		•	•	:	•		•	•		•
TGT	AAG	CAA	AAT	GIT	AGC	AGC	CIT	GAT	GAA	AAA	- <del>A</del> AT	AGC	GTT	TCA	GTA .
ACA	Tre	GIT	TTA	UAA	100	100	LAN	CTA	CIT	TIT	TTA	TCG	CAA	AGT	CAT
Cys	ьys	GIII	Wali	Val	261	261	rea	АБР	GIU	Lys	ASD	Ser	Val	Ser	Val>
1	00		1	110			120			1:	30			140	
	•	•		•		•	•		•		•	•		•	
GAT	TTA	CCT	GGT	GGA	ATG	ACA	GTT	CTT	GTA	AGT	AAA	GAA	AAA	GAC	አሕአ
CTA	AAT	GGA	CCA	CCT	TAC	TGT	CAA	GAA	CAT	TCA	TTT	CTT	TTT	CTG	TTT
ASP	ren	Pro	GIA	GIA	met	Thr	Vai	Leu	Val	Ser	Lys	Glu	Lys	Asp	Lys>
	150			16	50		1	170			180			19	90
•	•		•		•	•		•		•	•		•		•
GAC	GGT	AAA	TAC	AGT	CTA	GAG	GCA	ACA	GTA	GAC	AAG	CTT	GAG	CTT	AAA
CTG	CCA	TTT	ATG	TCA	GAT	CTC	CGT	TGT	CAT	CTG	TTC	GAA	CTC	GAA	TTT
Asp	GIA	Lys	Tyr	Ser	Leu	Glu	Ala	Thr	Val	Asp	Lys	Leu	Glu	Leu	Lys>
•	;	200			210			22	20		•	230			240
•		•		•	•		•		•	•		•		•	•
GGA	ACT	TCT	GAT	AAA	AAC	AAC	GGT	TCT	GGA	ACA	CTT	GAA	GGT	GAA	AAA
CUT	The	AGA	ACD	777	TTG	TTG	CCA	AGA	CCT	TGT	GAA	CTT	CCA	CTT	TII
Gly	1111	'26T	ASP	rys	ASI	ASI	GIA	ser	GIÀ	Inr	Leu	Glu	Gly	Glu	Lys>
		25	50		2	260		_	270			.28	30		
ልርጥ	GAC	444	ACT	-	СТА		ጥጥል	3 C N	אייי	CCT	CAT	C10	~	AGT	
TGA	CTG	TTT	TCA	TTT	CAT	TTT	AAT	TGT	TAA	CCA	CTA	CTC	CIA	TCA	CAA
Thr	Asp	Lys	Ser	Lys	Val	Lys	Leu	Thr	Ile	Ala	Asp	Asp	Leu	Ser	Glr>
				-										-	01117
290			300			31	10	_	3	320		_	330		
λСΤ	222	- -	CAA	እጥጥ	44C		CAA	CATT	CCC	•		-		TCA	•
TGA	TTT	AAA	CTT	TAA	AAG	TTT	CTT	CTA	CCC	TTTT	TOT	TIA	GIA	AGT	AAA
Thr	Lys	Phe	Glu	Ile	Phe	Lvs	Glu	Asp	Ala	LVS	Thr	TAN	Ua l	AGT.	Lys>
						-•			****	_, _	••••			Jei	Ly 37
.34	10	•	3	50			360		370			380			
		_		-		-	-		-		•	•		•	
AAA	GTA	ACC	حبب	444	CAC	244	ጥርአ	TCA	202	CAA	C 2 2		mma		~
AAA	GTA CAT	ACC TGG	CTT GAA	AAA TTT	GAC CTG	AAG TTC	TCA AGT	TCA AGT	ACA TCT	GAA	GAA CTT	እእእ ጉጉጉ	OTT O44	AAC	GAA
TTT	CAT	TGG	GAA	TTT	CTG	TTC	AGT	AGT	TGT	CTT	CTT	TTT	AAG	TTG	GAA CTT Glu>

FIGURE 23 (1 of 3)

WO 95/12676 PCT/US94/12352

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K48 OSP A/ PGAU OSPA FUSION

420 430 400 AAG GGT GAA ACA TCT GAA AAA ACA ATA GTA AGA GCA AAT GGA ACC AGA TTC CCA CTT TGT AGA CTT TTT TGT TAT CAT TCT CGT TTA CCT TGG TCT Lys Gly Glu Thr Ser Glu Lys Thr Ile Val Arg Ala Asn Gly Thr Arg> 460 470 450 440 CTT GAA TAC ACA GAC ATA AAA AGC GAT GGA TCC GGA AAA GCT AAA GAA GAA CTT ATG TGT CTG TAT TTT TCG CTA CCT AGG CCT TTT CGA TTT CTT Leu Glu Tyr Thr Asp Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu> 500 510 520 490 GTT TTA AAA GAC TTT ACT CTT GAA GGA ACT CTA GCT GCT GAC GGC AAA CAA AAT TTT CTG AAA TGA GAA CTT CCT TGA GAT CGA CGA CTG CCG TTT Val Leu Lys Asp Phe Thr Leu Glu Gly Thr Leu Ala Ala Asp Gly Lys> 570 550 540 530 ACA ACA TTG AAA GTT ACA GAA GGC ACT GTT GTT TTA AGC AAG AAC ATT TGT TGT AAC TTT CAA TGT CTT CCG TGA CAA CAA AAT TCG TTC TTG TAA Thr Thr Leu Lys Val Thr Glu Gly Thr Val Val Leu Ser Lys Asn Ile> 600 610 620 590 TTA AAA TCC GGA GAA ATA ACA GTT GCA CTT GAT GAC TCT GAC ACT ACT AAT TIT AGG CCT CTT TAT TGT CAA CGT GAA CTA CTG AGA CTG TGA TGA Leu Lys Ser Gly Glu Ile Thr Val Ala Leu Asp Asp Ser Asp Thr Thr> 650 660 640 CAG GCT ACT AAA AAA ACT GGA AAA TGG GAT TCA AAA ACT TCT ACT TTA GTC CGA TGA TTT TTT TGA CCT TTT ACC CTA AGT TTT TGA AGA TGA AAT Gln Ala Thr Lys Lys Thr Gly Lys Trp Asp Ser Lys Thr Ser Thr Leu> 720 700 710 690 ACA ATT AGT GTT AAC AGC AAA AAA ACT ACA CAA CTT GTG TTT ACT AAA TGT TAA TCA CAA TTG TCG TTT TTT TGA TGT GTT GAA CAC AAA TGA TTT Thr Ile Ser Val Asn Ser Lys Lys Thr Thr Gln Leu Val Phe Thr Lys> 740 750 CAA TAC ACA ATA ACT GTA AAA CAA TAC GAC TCC GCA GGT ACC AAT TTA GTT ATG TGT TAT TGA CAT TTT GTT ATG CTG AGG CGT CCA TGG TTA AAT Gln Tyr Thr Ile Thr Val Lys Gln Tyr Asp Ser Ala Gly Thr Asn Leu>

FIGURE 23 (2 of 3)

#### K48 OSPA / PGAU OSP A FUSION

770 780 790 800 810

GAA GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT
CTT CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA
Glu Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asr. Ala>

820

TTA AAA TAA AAT TTT ATT Leu Lys \*\*\*>

FIGURE 23 (3 of 3)

## B-31 OSP A /PGAU OSP A FUSION

		,	.0			20			30			4	0		•
	•		•	•		•		•	•		•		•	•	
ATG	AAA	AAA	TAT	ATT	TTG	GGA	ATA	GGT	CTA	ATA	TTA	GCC	TTA	ATA	GCA
			1 m 1	2 2 7	N N C	CCT	TAT	CCA	GAT	111	WWI	COG	w	111	CGI
Met	Lys	Lys	Tyr	Leu	Leu	Gly	Ile	Gly	Leu	lle	Leu	Ala	Leu	me	Ala>
							70			80			90		
50			60		•		•	•		•		•	•		• .
wcc	אאל	CNA	דע ג	GTT	AGC	AGC	CTT	GAT	GAA	ŽŽŽ	AAC	AGC	GCT	TCA	GTA
			mm a	C 2 2	TCC	TCG	GAA	CTA	CII	7.1.1	110	160	CGA	VO 1	C-11-1
\ \ \ \ \ \	LVS	Gln	Asn	Val	Ser	Ser	Leu	Asp	Glu	Lys	Asn	Ser	Ala	Ser	Val>
C, C														140	
10	00			110			120			1	30		•	.40	•
	•	•		•		•	~TT		CT)	AGT	AAA	GAA	AAA	GAC	AAA
GAT	TTG	CCT	GGT	GAG	ATG	AAA ~~~	Cyy	CII	CAT	TCA	TTT	CTT	TTT	CTG	TTT
CTA	AAC	GGA	CLA	CIU	Mot	TVS	Val	Leu	Val	Ser	Lys	Glu	Lys	λsp	Lys>
Asp	Leu	PIC	GIY	GIU	Mec	טעט					•				
	150			1	60			170			180			1:	90
•			•		•	•		•		•	•		•		•
GAC	GGT	· AAC	TAC	AGI	CTA	AAG	GC#	, AC	GT	A GAC	AAG	ATT	, GYC	CTA	እአል ፕፕፕ
		-	· • •	TC 1	רגם	` ጥጥር	, CC1	TG	CA:	CIU	111	. IAA	, 616	GWI	7 7 7
Asp	Gly	Lys	Tyr	Ser	Let	Lys	: Ala	Thi	· Va.	L ASE	Lys	: 11e	GIU	Leu	Lys>
					210	,		•	220			230			240
		200		•	,		•		•	•	•	•		•	•
CC3	אריי	ר ידכי	r GAT	נגג ז	A GA	C AAC	r GG	r TC	r GG	A GT	CT	C GAA	GG1	, ycy	<b>ጸ</b> ጸል . ፕፕፕ
			~~~		L (LL)	J 444		A AG	A CC		_ 644	4 (11		101	
Gly	Th	r Se	r Ası	Ly:	s As	p Asi	n G1;	y Se	r Gl	y Va	l Le	ı Glı	1 Gl}	Thr	Lys>
_									27				280		
			250			260		*	21	•		•	•	•	•
	•			ጥ አአ	, ,	מג ה	እ <b>ጥ</b> ፕ	a ac	TA A	T GC	T GA	C GA	T CT	A AGT	AAA 7
			m mc	× 4~	ጥ ሶር	ጥ ጥጥ	ጥ አአ	T TG	TTA	A CG	W CI	G C1	n un		
Δer	n As	n Lv	s Se	r Lv	s Al	a Ly	s Le	u Th	r Il	e Al	a As	p. As	p Le	ı Seı	Lys>
val	p no	p 23	•			_									
290			30	0			310			320			33	•	•
•		•.		•	•		•		* ~			· Y	a ct	י היאר:	A AGA
AC	C AC	A TI	C GA	A CI	TI	'A AA	IA GA	~~ ~	AT GO	יכ תיו	אר אני	T AA	T CA	C AG	A AGA T TCT
TG	G TO	T A	G CI	T GA	A A	Ti	re G1	la A	sn G	lv L	's Th	r Le	u Va	l Se	r Arg>
Th	r Tr	ar Pi	se Gi	u re	id De	։ս ւ	, 5 62		<b>.</b>	-, -,					
	340			350	)		31	50			370		•	380	
			•		•	•		•		•	•		•	•	
AA	A G	TA A	GT TO	T AC	GA G	AC A	A AA	CA T	CA A	CA G	AT G	AA A7	IC TI	C AA	T GAA
			~ > >/	~ N TT	<u>ጉጥ ሮ</u> ሳ	דה מי	יד די	CT A	GT T	GI C	IN C	T T T 1	4C A	10 11	A
Ly	s V	al S	er S	er A	rg A	sp L	ys T	hr S	er T	nr A	sp G	In -W	et Pl	ie va	n Glus

FIGURE 24 (1 of 3)

## B-31 OSP A/ PGAU OSP A FUSION

	,	390			40	0		4	10			420			43	C
	•	•		•		•	•		•		•	~ .		•		•
	AAA	GGT	GAA	TTG	TCT	GCA	AAA	ACC	ATG	ACA	AGA	GAA	AAT	COT	ACC	AAA ~~~
	TTT	CCA	CTT	AAC	AGA	CGT	TIT	TGG	TAC	101	10:	CIT	TIA	Cli	TGG	TIT
	Lys	Gly	Glu	Leu	Ser	Ala	Lys	Inr	met	Inr	Arg	GIU	ASD	GIA	inr	Lys>
		4	140		•	450			46	0		4	70			460
	•		•		•	•		•		•		~~	•		•	~
	CTT	GAA	TAT	ACA	GAA	ATG	AAA	AGC	GAT.	CCT	ACC	CCM	AAA	CC3	AAA	CAA
	GAA	CTT	ATA	TGT	CTT	TAC	TTT	TCG	CIA	CLI	100	CCI	Tue	NI n	TTT	Cli
	Leu	Glu	Tyr	Thr	GIU	met	гÀг	ser	Asp	GIY	1111	GIY	LYS	MIG	_ys	Glu>
			49	90		5	00			510			52	20		
		•		•	•		•		•	•		•		•	•	
	GTT	TTA	AAA	AAG	TTT	ACT	CTT	GAA	GGA	AAA	GTA	GCT	AAT	GAT	AAA	GTA
	CAA	AAT	TTT	TTC	AAA	TGA	GAA	CTT	CCT	TTT	CAT	CGA	TTA	CTA	TIT	CAT
	Val	Leu	Lys	Lys	Phe	Thr	Leu	Glu	Gly	Lys	Val	λla	Asn	Asp	Lys	Val>
	530			540			5	50		9	560			570		
	•		•	•		•		•	*		•		•	•		•
	ACA	TTG	GAA	GTA	AAA	GAA	GGA	ACC	GTT	ACT	TTA	AGT	AAG	GAA	ATT	GCA
	TGT	AAC	CTT	CAT	TTT	CTT	CCT	TGG	CAA	TGA	AAT	TCA	TTC	CTT	TAA	CGT
	Thr	Leu	Glu	Val	Lys	Glu	Gly	Thr	Val	Thr	Leu	Ser	Lys	Glu	Ile	Ala>
	5	во			590			600			6	10		(	620	
	_	•	•		•		•	•		•		•	•		•	
	AAA	TCT	GGA	GAA	• GTA	ACA	• GTT	• GCT	CTT	AAT	GAC	• ACT	AAC	ACT	ACT	CAG
	AAA TTT	TCT	CCT	GAA CTT	GTA CAT	TGT	CAA	GCT CGA	GAA	TTA	GAC CTG	ACT TGA	TTG	ACT TGA	ACT TGA	GTC
٠	AAA TTT	TCT	CCT	GAA CTT	GTA CAT	TGT	CAA	GCT CGA	GAA	TTA	GAC CTG	ACT TGA	TTG	ACT TGA	ACT TGA	CAG GTC Glm>
	AAA TTT	TCT	CCT	GAA CTT	GTA CAT Val	TGT	CAA	GCT CGA Ala	GAA	TTA	GAC CTG	ACT TGA	TTG	ACT TGA	ACT TGA Thr	GTC
	AAA TTT Lys	TCT AGA Ser	Gly	GAA CTT Glu	GTA CAT Val	TGT Thr 40	CAA Val	GCT CGA Ala	GAA Leu 650	TTA Asn	GAC CTG Asp	ACT TGA Thr	TTG Asn	ACT TGA Thr	ACT TGA Thr	GTC Glm>
	AAA TTT Lys	TCT AGA Ser 630	Gly	GAA CTT Glu	GTA CAT Val 6	TGT Thr 40 GGC	CAA Val	GCT CGA Ala	GAA Leu 650 GAT	TTA Asn	GAC CTG Asp	ACT TGA Thr 660	TTG Asn TCT	ACT TGA Thr	ACT TGA Thr 6	GTC Glm> 70 * ACA
	AAA TTT Lys • GCT CGA	TCT AGA Ser 630	Gly AAA	GAA CTT Glu AAA	GTA CAT Val 6 ACT TGA	TGT Thr 40 GGC CCG	CAA Val GCA	GCT CGA Ala TGG	GAA Leu 650 GAT CTA	TTA Asn TCA AGI	GAC CTG Asp	ACT TGA Thr 660 ACT	TTG Asn TCT AGA	ACT TGA Thr • ACT TGA	ACT TGA Thr 6°	GTC Glm> 70 * ACA TGT
	AAA TTT Lys • GCT CGA	TCT AGA Ser 630	Gly AAA	GAA CTT Glu AAA	GTA CAT Val 6 ACT TGA	TGT Thr 40 GGC CCG	CAA Val GCA	GCT CGA Ala TGG	GAA Leu 650 GAT CTA	TTA Asn TCA AGI	GAC CTG Asp	ACT TGA Thr 660 ACT	TTG Asn TCT AGA	ACT TGA Thr • ACT TGA	ACT TGA Thr 6°	GTC Glm> 70 * ACA
	AAA TTT Lys • GCT CGA	TCT AGA Ser 630	Gly AAA	GAA CTT Glu AAA	GTA CAT Val 6 ACT TGA	TGT Thr 40 GGC CCG	CAA Val GCA CGT Ala	GCT CGA Ala TGG	GAA Leu 650 GAT CTA Asp	TTA Asn TCA AGI	GAC CTG Asp	ACT TGA Thr 660 ACT TGA Thr	TTG Asn TCT AGA	ACT TGA Thr • ACT TGA	ACT TGA Thr 6°	GTC Glm> 70 * ACA TGT
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA	CCT Gly AAA TTT Lys	GAA CTT Glu AAA TTT Lys	GTA CAT Val 6 ACT TGA Thr	TGT Thr 40 GGC CCG Gly	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC	GAA Leu 650 GAT CTA Asp	TTA Asn TCA AGT Sex	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA	TTG Asn TCT AGA Ser 710	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 6 TTA AAT Leu	GTC Glm> 70 ACA TGT Thr>
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCT Gly AAA TTT Lys 680	GAA CTT Glu	GTA CAT Val  6 ACT TGA Thr	TGT Thr 40 GGC CCG Gly 690	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA ASP	TTA ASD TCA AGI Ser	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TTG Asn TCT AGA Ser 710	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 6' TTA AAT Leu	GTC Glm> 70 * ACA TGT Thr> 720 *
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCT Gly AAA TTT Lys 680	GAA CTT Glu . AAA TTT Lys	GTA CAT Val  6 ACT TGA Thr	TGT Thr  40 GGC CCG Gly 690	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA Asp 7	TCA AGT Ser	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA TGA Thr	TCT AGA Ser	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 6' TTA AAT Leu AAA TTT	GTC Gln> 70 ACA TGT Thr> 720 CAA GTT
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCT Gly AAA TTT Lys 680	GAA CTT Glu . AAA TTT Lys	GTA CAT Val  6 ACT TGA Thr	TGT Thr  40 GGC CCG Gly 690	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA Asp 7	TCA AGT Ser	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA TGA Thr	TCT AGA Ser	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 6' TTA AAT Leu AAA TTT	GTC Glm> 70 * ACA TGT Thr> 720 *
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCT Gly AAA TTT Lys 680 T GTT A CAA	GAA CTT Glu . AAA TTT Lys	GTA CAT Val  6 ACT TGA Thr	TGT Thr  40 GGC CCG Gly 690	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA Asp 7	TCA AGT Ser	GAC CTG ASP AAA TTT Lys	ACT TGA Thr 660 ACT TGA TGA Thr	TCT AGA Ser 710 . TTT AAA Phe	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 6' TTA AAT Leu AAA TTT	GTC Gln> 70 ACA TGT Thr> 720 CAA GTT
	AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thi	CCT Gly AAA TTT Lys 680 GTI A CAA	GAA CTT Glu . AAA TTT Lys . AAC . TTO . Asr	GTA CAT Val  6 ACT TGA Thr	TGT Thr  40 GGC CCG Gly 690 AAA TTI Lys	GCA Val GCA CGT Ala XAA TTI Lys	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA ASP 7 ACA TGI	TCA AST AGT Ser OO CAA GTT	GAC CTG ASP AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr CAC Val	TCT AGA Ser 710 • TTT AAA Phe	ACT TGA Thr ACT TGA Thr TGA Thr	ACT TGA Thr 6° TTA AAT Leu AAA TTT Lys	GTC Gln> 70 ACA TGT Thr> 720 CAA GGTT Gln>
	AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thi	CCT Gly AAA TTT Lys 680 CAA CAA	GAA CTT Glu AAA TTT Lys AAC	GTA CAT Val  6 ACT TGA Thr	TGT Thr  40 CCG Gly 690 AAA TTI Lys	GCA Val GCA CGT Ala AAA TTI Lys 740	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA ASP 7 ACA TGI Thi	TTA Asn TCA AGT Ser 00 CAM GTT 750	GAC CTG ASP AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr CAC Val	TTG ASN  TCT AGA Ser  710 • TTT AAA Phe	ACT TGA Thr ACT TGA Thr TGA Thr	ACT TGA Thr 6° TTA AAT Leu AAA TIT Lys	GTC Gln> 70 ACA TGT Thr> 720 CAA GTT Gln>
	AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thi	CCT Gly AAA TTT Lys 680 CAA CAA CAA T TA	GAA CTT Glu AAA TTT Lys AAC AAC	GTA CAT Val  6 ACT TGA Thr AGC TCG	TGT Thr  40 CCG Gly 690 AAA TTT	GCA Val GCA CGT Ala AAA TTT Lys 740 CAA CGT	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA ASP 7 ACA TGI Thi	TTA Asn TCA AGT Ser 00 CAM GTT TSI TSI TSI TSI TSI TSI TSI TSI TSI T	GAC CTG ASP AAA TTT Lys CTI GAA Lev	ACT TGA Thr 660 ACT TGA Thr CAC Val	TTG ASN TCT AGA Ser 710 • TTT AAA Phe 7	ACT TGA Thr ACT TGA Thr TGA Thr ACT TGA Thr	ACT TGA Thr 6° TTA AAT Leu AAA TIT Lys	GTC Gln> 70 ACA TGT Thr> 720 CAA GGTT Gln>

FIGURE 24 (2 of 3)

B-31 OSP A /PGAU OSP A FUSION

770 780 790 800 810

GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT TTA

CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA AAT

Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asn Ala Leu>

820

AAT AAA TTA TTT

Lys \*\*\*>

45/133

B31/K48 fusion 20 ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TIT TIT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala> 80 90 60 TGT AAG CAA AAT GTT AGC AGC CTT GAC GAG AAA AAC AGC GTT TCA GTA ACA TTC GTT TTA CAA TCG TCG GAA CTG CTC TTT TTG TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val> 130 120 110 GAT TTG CCT GGT GAA ATG AAA GTT CTT GTA AGC AAA GAA AAA AAC AAA CTA AAC GGA CCA CTT TAC TTT CAA GAA CAT TCG TTT CTT TTT TTG TTT Asp Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asn Lys> 190 160 170 180 150 GAC GGC AAG TAC GAT CTA ATT GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCG TTC ATG CTA GAT TAA CGT TGT CAT CTG TTC GAA CTC GAA TTT Asp Gly Lys Tyr Asp Leu Ile Ala Thr Val Asp Lys Leu Glu Leu Lys> 230 240 220 200 GGA ACT TCT GAT AAA AAC AAT GGA TCT GGA GTA CTT GAA GGC GTA AAA CCT TGA AGA CTA TTT TTG TTA CCT AGA CCT CAT GAA CTT CCG CAT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Val Leu Glu Gly Val Lys> 270 280 260 250 GCT GAC AAA AGT AAA GTA AAA TTA ACA ATT TCT GAC GAT CTA GGT CAA CGA CTG TTT TCA TTT CAT TTT AAT TGT TAA AGA CTG CTA GAT CCA GTT Ala Asp Lys Ser Lys Val Lys Leu Thr Ile Ser Asp Asp Leu Gly Gln> 310 320 330 290 300 ACC ACA CTT GAA GTT TTC AAA GAA GAT GGC AAA ACA CTA GTA TCA AAA TGG TGT GAA CTT CAA AAG TTT CTT CTA CCG TTT TGT GAT CAT AGT TTT Thr Thr Leu Glu Val Phe Lys Glu Asp Gly Lys Thr Leu Val Ser Lys> 380 360 340 350

AAA GTA ACT TCC AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAT GAA TTT CAT TGA AGG TTT CTG TTC AGT AGT TGT CTT CTT TTT AAG TTA CTT Lys Val Thr Ser Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu>

390 400 410 420 430

AAA GGT GAA GTA TCT GAA AAA ATA ATA ACA AGA GCA GAC GGA ACC AGA TTT CCA CTT CAT AGA CTT TTT TAT TAT TGT TCT CGT CTG CCT TGG TCT Lys Gly Glu Val Ser Glu Lys Ile Ile Thr Arg Ala Asp Gly Thr Arg>

FIGURE 25 (1 of 2)

B31/K48 fusion 480 450 CTT GAA TAC ACA GGA ATT AAA AGC GAT GGA TCT GGA AAA GCT AAA GAG GAA CTT ATG TGT CCT TAA TTT TCG CTA CCT AGA CCT TTT CGA TTT CTC Leu Glu Tyr Thr Gly Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu> 520 500 510 GTT TTA AAA GGC TAT GTT CTT GAA GGA ACT CTA ACT GCT GAA AAA ACA CAN ANT TIT CCG ATA CAN GAN CIT CCT TGN GAT TGN CGN CIT TIT TGT Val Leu Lys Gly Tyr Val Leu Glu Gly Thr Leu Thr Ala Glu Lys Thr> 550 560 540 530 ACA TTG GTG GTT AAA GAA GGA ACT GTT ACT TTA AGC AAA AAT ATT TCA TGT AAC CAC CAA TTT CTT CCT TGA CAA TGA AAT TCG TTT TTA TAA AGT Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser> 600 610 590 580 AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala> 660 670 630 GCT ACT AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA CGA TGA TTT TTT TGA CGT CGA ACC TTA AGT TTT TGA AGG TGA AAT TGT Ala Thr Lys Lys Thr Ala Ala Trp Asn Ser Lys Thr Ser Thr Leu Thr> 720 700 710 680 690 ATT AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA TAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT Ile Ser Val Asn Ser Gln Lys Thr Lys Asn Leu Val Phe Thr Lys Glu> 760 750 730 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA GAA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT CTT Asp Thr Ile Thr Val Gln Lys Tyr Asp Ser Ala Gly Thr Asn Leu Glu> 780 800 810 770

820

AAA TAA TTT ATT Lys \*\*\*>

GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

PCT/US94/12352

WO 95/12676

47/133

### B-31 OSP A/ 25015 OSP A FUSION

	10		20			30			-4	10		
•	• •		•		•	•		•		•	•	
ATG AAA AAA												
TAC TTT TTT												
Met Lys Lys	Tyr Leu	Leu	Gly	He	GIA	Leu	116	Leu	ATS	ren	ile	Ala>
50	60		7	0			80			90		
. • •	•	•	•	*	•		•		•	•		•
TGT AAG CAA	AAT GTT	AGC	AGC	CTT	GAC	GAG	AAA	AAC	AGC	GTT	TCA	GTA
ACA TTC GTT												
Cys Lys Gln	Asn Val	Ser	Ser	Leu	Asp	Glu	Lys.	.Asn	Ser	Val	Ser	Val>
				•••			• •	. ^				
100	110			120			13	30	•		140	
GAT TTG CCT	GGT GAA	ATG	AAA	GTT	CTT	GTA	AGC	AAA	GAA	AAA	AAC	AAA
CTA AAC GGA												
Asp Leu Pro												
-												
150	1	60	_	3	.70			180		_	19	90
GAC GGC AAG	* ************************************	-	) TOTA	CC1	202	CTA	CNC	220	CTT	CNC		•
CTG CCG TTC												
Asp Gly Lys												
	-,						•	•				-, -
200		210			22	20		:	230			240
• •	•	•		•		•	•		•		•	•
GGA ACT TCT		AAC			TCT	• GGA		CTT	GAA			AAA
GGA ACT TCT	CTA TTT	AAC TTG	TTA	CCT	TCT AGA	GGA CCT	CAT	CTT GAA	GAA CTT	CCG	CAT	AAA TTT
GGA ACT TCT	CTA TTT	AAC TTG	TTA	CCT	TCT AGA	GGA CCT	CAT	CTT GAA	GAA CTT	CCG	CAT	AAA TTT
GGA ACT TCT CCT TGA AGA Gly Thr Ser	CTA TTT	AAC TTG Asn	TTA	CCT	TCT AGA	GGA CCT	CAT	CTT GAA	GAA CTT Glu	CCG	CAT	AAA TTT
GGA ACT TCT CCT TGA AGA Gly Thr Ser	CTA TTT Asp Lys	AAC TTG Asn	TTA Asn 260	CCT	TCT AGA Ser	GGA CCT Gly 270	CAT Val	CTT GAA Leu	GAA CTT Glu	CCG Gly 80	CAT Val	AAA TTT Lys>
GGA ACT TCT CCT TGA AGA Gly Thr Ser 2	CTA TTT Asp Lys 50 AGT AAA	AAC TTG Asn	TTA Asn 260 AAA	CCT Gly TTA	TCT AGA Ser	GGA CCT Gly 270	CAT Val	CTT GAA Leu GAC	GAA CTT Glu 2 GAT	CCG Gly 80 • CTA	CAT Val	AAA TTT Lys>
GGA ACT TCT CCT TGA AGA Gly Thr Ser  2 GCT GAC AAA CGA CTG TTT	CTA TTT Asp Lys 50 AGT AAA	AAC TTG Asn	TTA ASD 260 AAA TTT	CCT Gly TTA AAT	TCT AGA Ser ACA TGT	GGA CCT Gly 270 ATT TAA	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 2 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val	AAA TTT Lys>
GGA ACT TCT CCT TGA AGA Gly Thr Ser 2	CTA TTT Asp Lys 50 AGT AAA	AAC TTG Asn	TTA ASD 260 AAA TTT	CCT Gly TTA AAT	TCT AGA Ser ACA TGT	GGA CCT Gly 270 ATT TAA	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 2 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val	AAA TTT Lys>
GGA ACT TCT CCT TGA AGA Gly Thr Ser  2 GCT GAC AAA CGA CTG TTT Ala Asp Lys	ASP Lys  ASP Lys  AGT AAA  TCA TTT  Ser Lys	AAC TTG Asn	TTA Asn 260 AAA TTT Lys	CCT Gly TTA AAT	TCT AGA Ser ACA TGT	GGA CCT Gly 270 ATT TAA Ile	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 2 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val GGT CCA Gly	AAA TTT Lys>
GGA ACT TCT CCT TGA AGA Gly Thr Ser  2 GCT GAC AAA CGA CTG TTT	CTA TTT Asp Lys 50 AGT AAA	AAC TTG Asn	TTA Asn 260 AAA TTT Lys	CCT Gly TTA AAT Leu	TCT AGA Ser ACA TGT	GGA CCT Gly 270 ATT TAA Ile	CAT Val TCT AGA Ser	CTT GAA Leu GAC CTG	GAA CTT Glu 2 GAT CTA	CCG Gly 80 • CTA GAT Leu	CAT Val GGT CCA Gly	AAA TTT Lys>
GGA ACT TCT CCT TGA AGA Gly Thr Ser  GCT GAC AAA CGA CTG TTT Ala Asp Lys  290 ACC ACA CTT	CTA TTT ASP Lys 50 AGT AAA TCA TTT Ser Lys 300 GAA GTT	AAC TTG Asn GTA CAT Val	TTA Asn 260 AAA TTT Lys 3	CCT Gly TTA AAT Leu 10	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser 320	CTT GAA Leu GAC CTG Asp	GAA CTT Glu 2 GAT CTA Asp	CCG Gly 80 CTA GAT Leu 330	CAT Val GGT CCA Gly	AAA TTT Lys> CAA GTT Gln>
GGA ACT TCT CCT TGA AGA Gly Thr Ser  GCT GAC AAA CGA CTG TTT Ala Asp Lys  290 ACC ACA CTT TGG TGT GAA	CTA TTT ASP Lys 50 AGT AAA TCA TTT Ser Lys 300 GAA GTT CTT CAA	AAC TTG Asn GTA CAT Val	AAA TTT AAA TTT AAA TTT	CCT Gly TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser 320 AAA TTT	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 2 GAT CTA ASP	CCG Gly 80 CTA GAT Leu 330 GTA	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA TTT
GGA ACT TCT CCT TGA AGA Gly Thr Ser  GCT GAC AAA CGA CTG TTT Ala Asp Lys  290 ACC ACA CTT	CTA TTT ASP Lys 50 AGT AAA TCA TTT Ser Lys 300 GAA GTT CTT CAA	AAC TTG Asn GTA CAT Val	AAA TTT AAA TTT AAA TTT	CCT Gly TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser 320 AAA TTT	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 2 GAT CTA ASP	CCG Gly 80 CTA GAT Leu 330 GTA	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA TTT
GGA ACT TCT CCT TGA AGA Gly Thr Ser  GCT GAC AAA CGA CTG TTT Ala Asp Lys  290 ACC ACA CTT TGG TGT GAA Thr Thr Let	CTA TTT ASP Lys  50  AGT AAA TCA TTT Ser Lys  300  GAA GTT CTT CAA	AAC TTG Asn GTA CAT Val	AAA TTT AAA TTT AAA TTT	TTA AAT Leu  GAA CTT Glu	TCT AGA Ser ACA TGT Thr GAT CTA ASP	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser 320 AAA TTT Lys	CTT GAA Leu GAC CTG Asp ACA TGT	GAA CTT Glu 2 GAT CTA ASP	CCG Gly 80 CTA GAT Leu 330 GTA	GGT CCA Gly TCA AGT Ser	AAA TTT Lys> CAA GTT Gln> AAA TTT
GGA ACT TCT CCT TGA AGA Gly Thr Ser  GCT GAC AAA CGA CTG TTT Ala Asp Lys  290 ACC ACA CTT TGG TGT GAA	CTA TTT ASP Lys 50 AGT AAA TCA TTT Ser Lys 300 GAA GTT CTT CAA	AAC TTG Asn GTA CAT Val	AAA TTT AAA TTT AAA TTT	CCT Gly TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr GAT CTA ASP	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser 320 AAA TTT Lys	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 2 GAT CTA ASP	CCG Gly 80 CTA GAT Leu 330 GTA	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA TTT
GGA ACT TCT CCT TGA AGA Gly Thr Ser  GCT GAC AAA CGA CTG TTT Ala Asp Lys  290 ACC ACA CTT TGG TGT GAA Thr Thr Let	CTA TTT Asp Lys  50 AGT AAA TCA TTT Ser Lys  300 CGAA GTT CTT CAA Glu Val	AAC TTG Asn GTA CAT Val	TTA Asn 260 AAA TTT Lys AAA TTT Lys	TTA AAT Leu  GAA CTT Glu  360	TCT AGA Ser ACA TGT Thr GAT CTA ASP	GGC CCG Gly	TCT AGA Ser 320 AAA TTT Lys	CTT GAA Leu GAC CTG ASP ACA TGT Thr	GAA CTT Glu 2 GAT CTA Asp	CCG Gly 80 CTA GAT Leu 330 GTA CAT Val	GGT CCA Gly TCA AGT Ser	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>
GGA ACT TCT CCT TGA AGA Gly Thr Ser  GCT GAC AAA CGA CTG TTT Ala Asp Lys  290  ACC ACA CTT TGG TGT GAA Thr Thr Lev  340	CTA TTT Asp Lys  50 AGT AAA TCA TTT Ser Lys  300 CTA CAT Glu Val  350 TCC AAA	AAC TTG ASn GTA CAT Val TTC AAG Phe	AAA TTT Lys AAA TTT Lys AAA TTT Lys	TTA AAT Leu  GAA CTT Glu  360	TCT AGA Ser ACA TGT Thr GAT CTA ASP	GGA CCT Gly 270 . ATT TAA Ile GGC CCG Gly	TCT AGA Ser 320 AAA TTT Lys 3	CTT GAA Leu GAC CTG ASP ACA TGT Thr	GAA CTT Glu 2 GAT CTA ASP CTA GAT Leu	CCG Gly 80 CTA GAT Leu 330 GTA CAT Val	GGT CCA Gly TCA AGT Ser 380	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>

FIGURE 26 (1 of 3)

### B-31 OSP A/ 25015 OSP A FUSION

	390 AA GGT GAA			40	00	•	4	110			420		•	43	30
		GAA													
															Arg>
·•	4	140		•	450		•	46	50	•	4	170		•	480
		TAC													
		ATG Tyr													Glu>
		49	90		9	500			510			52	20		
GTT	TTA	ааа	GGC	TAT	GTT	CTT	GAA	GGA	ACT	CTA	T.	GCT	GAA	444	ACA
		TTT													
Val	Leu	Lys	Gly	Tyr	Val	Leu	Glu	Gly	Thr	Leu	Thr	Ala	Glu	Lys	Thr>
530			540			55	50		9	560			570		
•	mmc.	· cmc	•		·	CC.	*	• •	<b>1</b> Cm	* ************************************		•	•		•
		GTG CAC													
		_													Ser>
50	30		:	590		_	600			63	10	_	(	520	
	•	• GGG		•	TCA	• GTT	•	CTT	AAT		•	• GAC		•	GCT
AAA TTT	• TCT AGA	GGG CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA
AAA TTT	• TCT AGA	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	
AAA TTT	• TCT AGA	CCC	GAA CTT	GTT CAA Val	AGT	CAA	GAA CTT Glu	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA Ala>
AAA TTT Lys	TCT AGA Ser 630	CCC Gly.	GAA CTT Glu	GTT CAA Val	AGT Ser 40 • GCA	CAA Val	GAA CTT Glu TGG	GAA Leu 550 • AAT	TTA Asn GCA	GAC CTG Asp	ACT TGA Thr 660	CTG Asp	AGT TCA Ser	AGT TCA Ser 67	CGA Ala>
AAA TTT Lys • GCT CGA	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu • AAA TTT	GTT CAA Val 64	AGT Ser 40 • GCA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 AAT TTA	TTA Asn GCA CGT	GAC CTG Asp	ACT TGA Thr 660 ACT TGA	CTG Asp TCA AGT	AGT TCA Ser • ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> CC ACA TGT
AAA TTT Lys • GCT CGA	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys	GAA CTT Glu • AAA TTT	GTT CAA Val 64	AGT Ser 40 • GCA CGT Ala	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 AAT TTA Asn	TTA Asn GCA CGT Ala	GAC CTG Asp	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCA AGT Ser	AGT TCA Ser • ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> CC ACA TGT Thr>
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	AAA TTT Lys	GAA CTT Glu • AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 550 AAT TTA Asn	GCA CGT Ala	GAC CTG Asp • GGC CCG Gly	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser	AGT TCA Ser • ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala>  CCA TGT Thr>  720
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	AAA TTT Lys 680	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 550 AAT TTA Asn 70	GCA CGT Ala	GAC CTG Asp GGC CCG Gly	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala>  CC ACA TGT Thr>  720 CAA
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr ACT TGA	AAA TTT Lys 680 GTA	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690 AAA TTT	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 550 AAT TTA Asn 70	GCA CGT Ala	GAC CTG Asp GGC CCG Gly CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser 710	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala>  CC ACA TGT Thr>  720 CAA
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr ACT TGA	AAA TTT Lys 680 GTA CAT Val	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 550 AAT TTA Asn 70	GCA CGT Ala	GAC CTG Asp GGC CCG Gly CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser 710 TTT AAA Phe	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala>  CC ACA TGT Thr>  720 CAA GTT
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr	AAA TTT Lys 680 GTA CAT Val	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTT CAA Val 64 ACT TGA Thr AAC TTG Asn	AGT Ser 40 GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp ACT TGA Thr	GAA Leu 550 AAT TTA ASD 70 AAA TTT Lys	GCA CGT Ala OCC CGG Ala 750	GAC CTG Asp GGC CCG Gly CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCA AGT Ser 710 TTT AAA Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala> CC ACA TGT Thr> 720 CAA GTT Gln>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr ACT TGA Thr	AAA TIT Lys 680 GTA CAT Val	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTT CAA Val 64 ACT TGA Thr AAC TTG Asn	AGT Ser 40 GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT Lys 740	GAA CTT Glu TGG ACC Trp ACT TGA Thr	GAA Leu 550 AAT TTA ASN 7 AAA TTT Lys	GCA CGT Ala 00 GCC CGG Ala 750	GAC CTG Asp GGC CCG Gly CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCA AGT Ser 710 TTT AAA Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala> CC ACA TGT Thr> 720 CAA GTT Gln>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr ACT TGA Thr	AAA TTT Lys 680 GTA CAT Val 7 ATT	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTT CAA Val 64 ACT TGA Thr AAC TTG ASn	AGT Ser 40 GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT Lys 740	GAA CTT Glu TGG ACC Trp ACT TGA Thr	GAA Leu 550 AAT TTA ASN 7 AAA TTT Lys GAC CTG	GCA CGT Ala OCC CGG Ala 750 TCA AGT	GAC CTG Asp GGC CCG Gly CTT GAA Leu GCA	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCA AGT Ser 710 TTT AAA Phe ACC TGG	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala> CC ACA TGT Thr> 720 CAA GTT Gln>

FIGURE 26 (2 of 3)

49//33

# B-31 OSP A/ 25015 OSP A FUSION

770 780 790 800 810

GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT TTA

CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA AAT

Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asn Ala Leu>

AGA TCT Arg>

FIGURE 26 (3 of 3)

## K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

		1	0		:	20			30			4	0		
	•		•	•		• `		•	•		•		•		
AŤG	AAA	AAA	TAT	ATT	TTG	GGA	ATA	GGT	CTA	ATA	TTA	GCC	ATT	ATA	GCA
				N N T	* * C	CCT	ירביד	CCA	ندامات	IVI	w	~00	,,,,,,	4 6 7 4	COL
Met	Lvs	Lys	Tyr	Leu	Leu	Gly	Ile	Gly	Leu	Ile	Leu	Ala	Leu	TTE	Ala>
	-3 -	-	_												
5Ó			60			7	0			80		_	90		•
•		•	•		•		•	•		•		300	-	mc s	CTA
TGT	AAG	CAA	AAT	GTT	AGC	AGC	CTT	GAT	GAA	AAA	AAT	AGC	GII	TCA	CIA
			mm l	~ ~ ~ ~	ጥርር	TCG	GAA	CIA	~11	771.	. 4 A W	100	CAN	701	C
Cys	Lys	Gln	Asn	Val	Ser	Ser	Leu	Asp	Glu	Lys	Asn	Ser	vaı	Ser	Val>
							120				30			140	
1	00			110			120		•	_	•	*		•	
	•			-	`mc	ACA	CTT	<b>CTT</b>	GTA	AGT	AAA	GAA	AAA	GAC	AAA
GAT	TTA	CCT	GGT	GGA	WIG	TGT	CYV	CII	CAT	TCA	TTT	CTT	TTT	CTG	TTT
CTA	AAT	GGA	CCA	CCI	MAC	The	Val	Len	Val	Ser	Lvs	Glu	Lys	Asp	Lys>
Asp	Leu	Pro	Gly	GIA	met	1111	VU.1	DCL					-	•	-
				1	60		•	170			180	)		1	90
_	150			_		•	•	•		•	•		•		•
			ጥአር	אכידי	СТА	GAG	GCA	ACA	GTA	A GAC	: AAG	CTT	GAG	CTT	AAA
		-		. TC >	CAT		്രസ	TGI	, CA	r Cr	, ,,,	. GAA		GAA	
CTG	CC/		- Tree	· 5e*	Leu	Glu	Ala	Thr	Va!	l Ası	Lys	Leu	Glu	Leu	Lys>
ASP	, 617	Lys	, 1 <b>71</b>				•								
		200			210	}		2	220			230			240
	,			•	•	•	•		•	,	•	•		•	•
GG:	AC'	r TC	r GA	KAA 1	A AAC	: AAC	GGT	TCT	r GG	A AC	A CT	r GA	GG7	GAA	ለጸ <i>ል</i> ጉጥጉ
			N (~T)	· 444	ዮ ጥጥር	ידר :	CCA	A AG	A CC	I IG	I GW	4 CT1	LCC		
GIV	· Th	r Se	r Ası	Lys	s Asi	a Asn	Gly	/ Sei	r G1	y Th	r Le	u Glu	ı Gly	, Gli	Lys>
02.	,														
			250			260			27	0		•	280		•
	•		•	,	•	•		•		<b>*</b>	m ca	m (C)	- <del>-</del>	א אכי	r C22
AC.	T GA	C AA	A AG	T AA	A GT	A AAA	\ TT	A AC	A A1	T GC	1 GA	7 CW	C CI	י אנט. די ארט	CAA CTT
TG	A CT	G TI	T TC	A TT	I CA	rTT	AA 1	r TG	T TA	A CG	y CI	W C1	n to	1 IO	A GTT
Th	r As	p Ly	s Se	r Ly	s Va	l Lys	s Le	מד ט	I II	e Al	a AS	p as	b pe	u 50.	r Gln>
			20	^			310			320	)		33	0	
290			30				•		•	1		•		•	•
			~ C		~T TV	C 77	A GA	A GA	T GC	C A	A AC	A TT	A GT	A TC	ል ልልል ተጥተ
		~ 1 1	~	ጥ ጥል	AAA	CTT	тст	тсі	ж ст	<b>3</b> 6 1.	TI	J AM		TAG	
TG	A	D	W CI		e Ph	e Iv	s G1	u As	D A	la Ly	s Th	ır Le	u Va	1 Se	r Lys>
Tr	n r?	/S PI	15 01		1	,			•	-				•	
	340			350	)		36	0			370			380	)
	_		•			•		•	,	•	•		•	•	
74.		TA A	ככ כי	TT AJ	AA GA	AC AA	G TC	CA TO	CA A	CA G	AA G	AA AA	LA T	C A	AC GAA
_	~	<b>A</b> TO	~~ ~	אף ממ	~T ~	רה הא	C AC	ST A	GT T	GT C	II C	** **		10 I	
1.5	vs V	al T	hr L	eu Ly	ys A:	sp Ly	's Se	er S	er T	hr G	lu G	lu Ly	ys Pl	ne A	sn Glu>

FIGURE 27 (1 of 3)

K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

430 400 390 AAG GGT GAA ACA TCT GAA AAA ACA ATA GTA AGA GCA AAT GGA ACC AGA TTC CCA CTT TGT AGA CTT TTT TGT TAT CAT TCT CGT TTA CCT TGG TCT Lys Gly Glu Thr Ser Glu Lys Thr Ile Val Arg Ala Asn Gly Thr Arg> 480 470 460 450 CTT GAA TAC ACA GAC ATA AAA AGC GAT GGA TCC GGA AAA GCT AAA GAA GAA CTT ATG TGT CTG TAT TTT TCG CTA CCT AGG-CCT TTT CGA TTT CTT Leu Glu Tyr Thr Asp Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu> 520 510 500 490 GTT TTA AAA GAC TTT ACT CTT GAA GGA ACT CTA GCT GCT GAC GGC AAA CAA AAT TTT CTG AAA TGA GAA CTT CCT TGA GAT CGA CGA CTG CCG TTT Val Leu Lys Asp Phe Thr Leu Glu Gly Thr Leu Ala Ala Asp Gly Lys> 560 550 530 ACA ACA TTG AAA GTT ACA GAA GGC ACT GTT GTT TTA AGC AAG ATT TCA TGT TGT AAC TTT CAA TGT CTT CCG TGA CAA CAA AAT TCG TTC TAA AGT Thr Thr Leu Lys Val Thr Glu Gly Thr Val Val Leu Ser Lys Ile Ser> 610 600 590 580 AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala> 650 670 660 640 630 GCT ACT AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA CGA TGA TTT TTT TGA CGT CGA ACC TTA AGT TTT TGA AGG TGA AAT TGT Ala Thr Lys Lys Thr Ala Ala Trp Asn Ser Lys Thr Ser Thr Leu Thr> 710 700 680 690 ATT AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA TAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT Ile Ser Val Asn Ser Gln Lys Thr Lys Asn Leu Val Phe Thr Lys Glu> 760 750 740 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA GAA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT CTT Asp Thr Ile Thr Val Gln Lys Tyr Asp Ser Ala Gly Thr Asn Leu Glu>

FIGURE 27 (2 of 3)

52/133

K48 OSP A / B-31 OSP A/ K48 OSP A FUSION

770 780 790 800 810

GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTA TTT

Lys \*\*\*>

# 53/133

# B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

		1	0			20			30			. 4	0		÷
ATC	*	ААА	• TAT	4. T.T.	<b>ተ</b> ሞር	400	ATA	• GGT	CTA	ATA	TTA	GCC	TTA	* 4TA	GC2
		TTT													
Met	Lys	Lys	Tyr	Leu	Leu	Gly	Ile	Gly	Leu	Ile	Leu	Ala	Leu	Ile	Ala>
50			60			-	10			80			90		
•		•	•		•		•	•		•		•	•		•
		CAA													
		GTT Gln													CAT.
-, -	-, -														
10	00	_	1	110			120			13	30		:	140	
GAT	TTA	CCT	GGT	GGA	ATG	ACA	GTT	CTT	GTA	AGT	AAA	GAA	AAA	GAC	AAA
		GGA													
Asp	Leu	Pro	Gly	Gly	Met	Thr	Val	Leu	Val	Ser	Lys	Glu	Lys	Asp	Lys>
	150			16	50		1	170			180			19	90
•	•		•		•	•		•		•	•		•		•
		AAA													
		TTT													Lys>
-	_	_	_								•				•
											_				
:		200			210		•	2:	20	•	1	230		•	240
; GGA		200 TCT	GAT	AAA	•	AAC	• GGT		•	ACA		•	GGT	• GAA	•
CCT	ACT TGA	TCT AGA	CTA	TTT	AAC TTG	TTG	CCA	TCT AGA	GGA CCT	TGT	CTT GAA	GAA CTT	CCA	CTT	AAA TTT
CCT	ACT TGA	TCT AGA	CTA	TTT	AAC TTG	TTG	CCA	TCT AGA	GGA CCT	TGT	CTT GAA	GAA CTT	CCA	CTT	AAA
CCT	ACT TGA	TCT AGA Ser	CTA	TTT	AAC TTG Asn	TTG	CCA	TCT AGA	GGA CCT	TGT	CTT GAA	GAA CTT Glu	CCA	CTT	AAA TTT
CCT Gly	ACT TGA Thr	TCT AGA Ser	CTA Asp 50	TTT Lys	AAC TTG Asn	TTG Asn 260	CCA Gly	TCT AGA Ser	GGA CCT Gly 270	TGT Thr	CTT GAA Leu	GAA CTT Glu	CCA Gly 30	CTT Glu	AAA TTT Lys>
CCT Gly ACT	ACT TGA Thr	TCT AGA Ser	CTA Asp 50 AGT	TTT Lys	AAC TTG Asn	TTG Asn 260 AAA	CCA Gly TTA	TCT AGA Ser	GGA CCT Gly 270	TGT Thr	CTT GAA Leu	GAA CTT Glu 21	CCA Gly 30 • CTA	CTT Glu	AAA TTT Lys>
CCT Gly ACT TGA	ACT TGA Thr GAC CTG	TCT AGA Ser 25	CTA ASP 50 AGT TCA	TTT Lys • AAA TTT	AAC TTG Asn GTA CAT	TTG Asn 260 AAA TTT	CCA Gly TTA AAT	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA	TGT Thr GCT CGA	CTT GAA Leu GAT CTA	GAA CTT Glu 21 GAC CTG	CCA Gly 30 CTA GAT	CTT Glu AGT TCA	AAA TTT Lys>
CCT Gly ACT TGA	ACT TGA Thr GAC CTG	TCT AGA Ser 25	CTA ASP 50 AGT TCA	TTT Lys • AAA TTT	AAC TTG Asn GTA CAT	TTG Asn 260 AAA TTT Lys	CCA Gly TTA AAT	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA	CTT GAA Leu GAT CTA	GAA CTT Glu 21 GAC CTG	CCA Gly 30 CTA GAT	CTT Glu AGT TCA	AAA TTT Lys>
CCT Gly ACT TGA Thr	ACT TGA Thr GAC CTG Asp	TCT AGA Ser 25 AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300	TTT Lys • AAA TTT Lys	AAC TTG Asn GTA CAT Val	TTG Asn 260 AAA TTT Lys	CCA Gly TTA AAT Leu	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA Ala	CTT GAA Leu GAT CTA Asp	GAA CTT Glu 2: GAC CTG Asp	CCA Gly 30 CTA GAT Leu 330	CTT Glu AGT TCA Ser	AAA TTT Lys> CAA GTT Gln>
CCT Gly ACT TGA Thr 290	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 2: AAA TTT Lys	CTA Asp 50 AGT TCA Ser 300	TTT Lys AAA TTT Lys	AAC TTG Asn GTA CAT Val	TTG Asn 260 AAA TTT Lys 3	CCA Gly TTA AAT Leu 10	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA Ala 320	CTT GAA Leu GAT CTA ASP	GAA CTT Glu 2 GAC CTG Asp	CCA Gly 30 CTA GAT Leu 330	CTT Glu AGT TCA Ser	AAA TTT Lys> CAA GTT Gln> AAA
CCT Gly ACT TGA Thr 290 ACT TGA	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 2: AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300 GAA CTT	TTT Lys AAA TTT Lys ATT TAA	AAC TTG Asn GTA CAT Val TTC AAG	TTG Asn 260 AAA TTT Lys 3	TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA Ala 320	CTT GAA Leu GAT CTA ASP	GAA CTT Glu 2 GAC CTG ASP	CCA Gly 30 CTA GAT Leu 330 GTA CAT	CTT Glu AGT TCA Ser TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA
ACT TGA Thr 290 ACT TGA Thr	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 2: AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300 GAA CTT Glu	TTT Lys AAA TTT Lys ATT TAA	AAC TTG Asn GTA CAT Val TTC AAG	TTG Asn 260 AAA TTT Lys 3	TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA Ala 320 AAA TTT Lys	CTT GAA Leu GAT CTA ASP	GAA CTT Glu 2 GAC CTG ASP	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	AGT TCA Ser TCA AGT Ser	AAA TTT Lys> CAA GTT Gln>
ACT TGA Thr 290 ACT TGA Thr	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 2: AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300 GAA CTT Glu	Lys  AAA TTT Lys  ATT TAA Ile	AAC TTG Asn GTA CAT Val TTC AAG	TTG Asn 260 AAA TTT Lys 3	TTA AAT Leu  GAA CTT Glu	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA Ala 320 AAA TTT Lys	CTT GAA Leu GAT CTA Asp	GAA CTT Glu 2 GAC CTG ASP	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	CTT Glu AGT TCA Ser TCA AGT	AAA TTT Lys> CAA GTT Gln>
ACT TGA Thr 290 ACT TGA Thr	ACT TGA Thr GAC CTG ASP AAA TTT Lys	TCT AGA Ser 2: AAA TTT Lys TTT AAA Phe	CTA ASP 50 AGT TCA Ser 300 CTT Glu	AAA TTT Lys ATT TAA Ile 350	AAC TTG Asn GTA CAT Val	TTG Asn 260 AAA TTT Lys AAA TTT Lys AAA ATTT AAA AAA AAA AAA	CCA Gly TTA AAT Leu 10 GAA CTT Glu 360	TCT AGA Ser . ACA TGT Thr . GAT CTA Asp	GGA CCT Gly 270 ATT TAA Ile GCC CGG Ala	GCT CGA Ala 320 AAA TTT Lys GAA	CTT GAA Leu GAT CTA ASP ACA TGT Thr	GAA CTT Glu 2: GAC CTG ASP TTA AAT Leu	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	AGT TCA Ser TCA AGT Ser 380	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>
ACT TGA Thr 290 ACT TGA Thr AAA	ACT TGA Thr GAC CTG ASP AAA TTT Lys	TCT AGA Ser  2: AAA TTT Lys  TTT AAA Phe ACC TGG	CTA ASP 50 AGT TCA Ser 300 GAA CTT Glu CTT GAA	AAA TTT Lys ATT TAA Ile 350 AAA TTT	AAC TTG Asn GTA CAT Val TTC AAG Phe GAC CTG	TTG Asn 260 AAA TTT Lys AAA TTT Lys AAA TTT Cys	CCA Gly TTA AAT Leu 10 GAA CTT Glu 360 • TCA	TCT AGA Ser ACA TGT Thr CTA ASp	GGA CCT Gly 270 ATT TAA Ile GCC CGG Ala	GCT CGA Ala 320 AAA TTT Lys GAA CTT	CTT GAA Leu GAT CTA Asp ACA TGT Thr	GAA CTT Glu 2 GAC CTG Asp TTA AAT Leu	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	AGT TCA Ser TCA AGT Ser 380	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>

FIGURE 28 (1 of 3)

# 54/133 B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

	390			40	0		4	10			420			43	30 .
•	•		•		•	•		. •	•	•	•		•		•
AAG	GGT	GAA	ACA	TCT	GAA	AAA	ACA	ATA	GTA	AGA	GCA	TAA	GGA	ACC	AGA
TTC	CCA	CTT	TGT	AGA	CTT	TTT	TGT	TAT	CAT	TCT	CGT	TTA	CCT	TGG	TCT
Lys	Gly	Glu	Thr	Ser	Glu	Lys	Thr	Ile	Val	Arg	Ala	Asn	Gly	Thr	Arg>
	4	140			450			46	50		4	170			480
•		•		•	. •		•		•			•		•	•
		TAC													
		ATG													
Leu	GIU	ıyr	Thr	ASP	116	Lys	ser	ASP	CIA	ser	GIĀ	rys	Ala	Lys	Glu>
		49	20			500			510			51	20		
	•	٧.	•	•	•	•		•	•		•	-	•	•	
GTT	TTA	AAA	GAC	TTT	ACT	CTT	GAA	GGA	ACT	СТА	GCT	GCT	GAC	GGC	AAA
		TTT													
															Lys>
530			540			55	50		5	560			570		
•		•	•		•		•	•		•		•	•		•
		TTG													
		AAC													
Thr	Thr	Leu	Lys	Val	Thr	Glu	Gly	Thr	Val	Val	Leu	Ser	Lys.	Ile	Ser>
51	80			590			600			6:	10		f	320	
51	B0 •	•	:	590		•	600		•	6:	10	•	€	520	
	•	• GGG		•	TCA	• GTT	•	CTT	• AAT		•	• GAC		•	GCT
ААА	• TCT	egg CCC	GAA	GTT			GAA			GAC	• ACT		AGT	• AGT	
AAA TTT	• TCT AGA	ccc	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	• ACT TGA	CTG	AGT TCA	AGT TCA	
AAA TTT	TCT AGA Ser	ccc	GAA CTT	GTT CAA Val	AGT Ser	CAA	GAA CTT Glu	GAA Leu	TTA	GAC CTG	ACT TGA Thr	CTG	AGT TCA	AGT TCA Ser	CGA Ala>
AAA TTT	• TCT AGA	ccc	GAA CTT	GTT CAA Val	AGT	CAA	GAA CTT Glu	GAA	TTA	GAC CTG	• ACT TGA	CTG	AGT TCA	AGT TCA Ser	CGA
AAA TTT Lys	TCT AGA Ser 630	CCC	GAA CTT Glu	GTT CAA Val	AGT Ser	CAA Val	GAA CTT Glu	GAA Leu 650	TTA Asn	GAC CTG Asp	ACT TGA Thr	CTG Asp	AGT TCA Ser	AGT TCA Ser	CGA Ala>
AAA TTT Lys • GCT	TCT AGA Ser 630 ACT	CCC Gly	GAA CTT Glu	GTT CAA Val 6-	AGT Ser 40 • GCA	CAA Val	GAA CTT Glu TGG	GAA Leu 650 *	TTA Asn TCA	GAC CTG Asp	ACT TGA Thr 660	CTG Asp	AGT TCA Ser	AGT TCA Ser 67	CGA Ala> 70 * ACA
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu • AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 40 GCA CGT	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA	TTA Asn TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT	CTG Asp TCC AGG	AGT TCA Ser • ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> 70 * ACA TGT
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu • AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 40 GCA CGT	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA	TTA Asn TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT	CTG Asp TCC AGG	AGT TCA Ser • ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> 70 * ACA
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu • AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 40 GCA CGT	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 * AAT TTA Asn	TTA Asn TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCC AGG	AGT TCA Ser • ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> 70 * ACA TGT
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT Lys	GAA CTT Glu • AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 40 • GCA CGT Ala	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 * AAT TTA Asn	TTA Asn TCA AGT Ser	GAC CTG Asp	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCC AGG Ser	AGT TCA Ser • ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> 70 ACA TGT Thr>
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys	GAA CTT Glu • AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Txp	GAA Leu 650 AAT TTA Asn	TTA Asn TCA AGT Ser	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser • ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr>
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 650 * AAT TTA Asn 7	TTA Asn TCA AGT Ser	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr>
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr AGT TCA	AAA TTT Lys 680 GTG	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr AGC TCG	AGT Ser 40 GCA CGT Ala 690 CAA GTT	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Txp	GAA Leu 550 AAT TTA Asn 7	TTA Asn TCA AGT Ser 00 AAC	GAC CTG Asp AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala> 70 ACA TGT Thr> 720
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr AGT TCA	AAA TTT Lys 680 GTG CAC Val	GAA CTT Glu AAA TTT Lys AAT TTA ASD	GTT CAA Val 64 ACT TGA Thr AGC TCG	AGT Ser 40 • GCA CGT Ala 690 • CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Txp	GAA Leu 550 AAT TTA Asn 7	TTA Asn TCA AGT Ser 00 AAC TTG Asn	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser 710 TTC AAG	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr AGT TCA	AAA TTT Lys 680 GTG CAC Val	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr AGC TCG	AGT Ser 40 • GCA CGT Ala 690 • CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Txp	GAA Leu 550 AAT TTA Asn 7	TTA Asn TCA AGT Ser 00 AAC	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser 710 TTC AAG	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 . ACT TGA Thr AGT TCA Ser	AAA TTT Lys 680 GTG CAC Val	GAA CTT Glu AAA TTT Lys AAT TTA Asn	GTT CAA Val 64 ACT TGA Thr AGC TCG Ser	AGT Ser  40  GCA CGT Ala  690  CAA GTT Gln	GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp ACC TGG	GAA Leu 650 AAT TTA Asn 7 AAA TTT Lys	TTA Asn TCA AGT Ser 00 AAC TTG Asn 750	GAC CTG Asp AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser 710 • TTC AAG Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser ACA	AAA TTT Lys 680 GTG CAC Val	GAA CTT Glu AAA TTT Lys AAT TTA Asn	GTT CAA Val 60 ACT TGA Thr AGC TCG Ser	AGT Ser  40  GCA CGT Ala  690  CAA GTT Gln	CAA Val  GCT CGA Ala  AAA TTT Lys 740 AAA	GAA CTT Glu TGG ACC Trp ACC TGG Thr	GAA Leu 550 AAT TTA ASN 7 AAA TTT Lys	TTA ASN TCA AGT Ser 00 AAC TTG ASN 750	GAC CTG Asp AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser TTC AAG Phe 7	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu . AAA TTT Lys . CTA	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 . ACT TGA Thr TCA Ser ACA TGT	AAA TTT Lys 680 GTG CAC Val 7	GAA CTT Glu AAA TTT Lys AAT TTA Asn	GTT CAA Val 64 ACT TGA Thr AGC TCG Ser GTA CAT	AGT Ser  40  GCA CGT Ala  690  CAA GTT Gln  CAA GTT	CAA Val GCT CGA Ala AAA TTT Lys 740 AAA TTT	GAA CTT Glu TGG ACC Trp ACC TGG Thr	GAA Leu 550 AAT TTA ASN 7 AAA TTT Lys	TTA ASN TCA AGT Ser 00 AAC TTG ASN 750 TCA	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser TTC AAG Phe ACC TGG	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys CTA GAT	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>

FIGURE 28 (2 of 3)

#### B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

770 780 790 800 610

GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA
CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT
Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys \*\*\*>

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## B-31 OSPA/ B-31 OSPB FUSION

		3.0			20			30				40			
		10		•		•		•	•		•		•	•	
N 1770	222	222	ТАТ	TTA	TTG	GGA	ATA	GGT	CTA	ATA	TTA	GCC	TTA AAT	ATA	GCA
Mar	IVS	LVS	Tvr	Leu	Leu	Gly	Ile	Gly	Leu	Ile	Leu	·Ala	Leu	Ile	Ala>
Mec	<i>D</i> 3 <i>D</i>	٠,٠	-,-												
50			60			•	70			80		_	90		
		•	•		•		•	•		•			~~~	~C N	CTA :
TGT	AAG	CAA	AAT	GTT	AGC	AGC	CTT	GAC	GAG	AAA	AAC	AGC	GII	AGT	GTA ·
				~ ~ ~ ~	$\mathcal{C}$	TCC	CAA	CTG	LIL		-1110	100		7101	~··
Cys	Lys	Gln	Asn	Val	Ser	Ser	Leu	ASP	GIU	Lys	W211	Jer	***		Val>
				- <b></b>			120			3	30			140	
1	00			110			120			•	•	•		•	
	•	•		- C. N	እጥር	- 444	GTT	CTI	GTA	AGC	AAA	GAA	AAA	AAC	AAA TTT
			~~1		ጥአር	TTTT	CYA	GAA	CAI	1.00	, 111	11	* * * *	110	
CTA	AAC	GGA	CLA	Cli	Met	INS	: Val	Lev	ı Val	Ser	Lys	Glu	Lys	Asn	Lys>
Asp	Let	Pro	, GIA	Giu	1100	٠, د									
	150	1		1	60			170			180	)		1	90
• ,			•			•	•	•		•	•	•	•		•
GAC	GG	AA C	OAT E	GAT	СТА	. ATT	GCA	A AC	A GT	A GA	AA :	CT	GAG	CTI	AAA TTT
					ר איז	ו מידיי	7 CC3	r TG	I CA	T. C.11	, ,,,	_ 0~	, -,,		
Asp	G1;	y Ly	s Ty	c Asp	Lev	Ile	Ala	A Th	r Va	l As	p Ly:	s Lei	ı Gıu	Leu	Lys>
									220			230			240
		200			210	)			220		•	-		•	•
•	•	• 		- ·		- אמ	r GG	A TC	T GG	A GT	A CT	T GA	A GG	GT	<b>AAA</b> TTT
					P 677	- 4	א כריי	T AG	A CL	T CA	JUN	~ ~ .		,	
CC.	r TG	A AG	~ yc	n tar	c Asi	n As	n Gl	v Se	r Gl	y Va	l Le	u Gl	u Gly	y Val	Lys>
GT.	y	1 36	1 V2	ינט ע				•							
			250			260			27	0			280		_
	•	•			•	•		•		•		· 	• 		
GC	T G	C A	A AG	T AA	A GT	A AA	A TT	A AC	CA AC	T TC	T G	C GA	T CT	A GG	T CAA
				· 2 ~~	ጥ ሮአ	ጥጥ	ጥ አአ	T TO	5T T#	A A	, A L I	$\iota \cup \iota$	A UA	1	
Al	a As	sp Ly	s Se	r Ly	s Va	1 Ly	s Le	u Ti	or 1.	te Se	er As	SP AS	ib re	u Gr	y Gln>
							220			320	1	•	33	0	
290	)		3(	00	_		310		•	32	*	•		•	•
•	·	•			~~ ~~ -	~ 11	A G	AA G	AT G	GC A	AA AA	CA C	ra Gi	A TO	AAA A:
				~~ ^1		J. J.	PT ("	L C.	TA C	CG T	11 1	GI G	<b>~</b> 1	,, ,,,	
T	3G T	GT G	AA C	11 U	i Pi	ne Li	s G	lu A	sp G	ly L	ys T	hr L	eu Va	al Se	r Lys>
TI	ir 1	11L P	-4 6	,,		,			-	-					
	340			35	0		3	60			370	•	,	380	)
			•		•	•		•		•	*		•		
A	AA G	A AT	CT T	CC A	AA G	AC A	AG T	CA I	CA A	CA G	AA G	AA A	AA T	rc A	AT GAA
						T-	ጥሮ አ	מידים	וי יויבאו	4 : 1 · (	1-r c	. 1 1 1	** *	no 4	44. —
L	ys \	al 1	hr S	er L	ys A	sp L	ys S	er S	ser 1	Thr C	stu C	iu L	ys P	ne A	sn Glu>
			_												

FIGURE 29 (1 of 3)

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B-31 OSP A/ B-31 OSP B FUSION

	390			40	0	_	4	10		•	420		•	43	0
TTT	CCA	CTT	CAT	AGA	CTT	TTT	ATA TAT	TAT	TGT	TCT	CGT	CTG	CCI	TG3	AGA TCT AIG>
Lys	_	40	vai.	361	450	<b>.</b>		46				70			480
•		•		•	•		•		•			•	~~~	•	•
CTT	GAA	TAC	ACA	GGA	ATT	AAA	AGC	GAT	GGA	TCT	GGA	AAA	GCT.	AAA	GAG
GAA	CTT	ATG	TGT	CCT	TAA	TTT	TCG	CTA	ču.	AGA	či.	111	Ala	lii	Glu>
Leu	Glu	Tyr	Thr	GIY	116	Lys	Ser	ASP	GIĀ	261	GIY	Lys	via	Lys	Gruz
		49	90		5	00			510			52	0 .		
	*		•	•		•		•	•		•		•	•	
GTT	TTA	AAA	GGC	TAT	GTT	CTT	GAA	GGA	ACT	CTA	ACT	GCT	GAA	AAA	ACA
CAA	TAA	TTT	CCG	ATA	CAA	GAA	CTT	CCL	TGA	LAN	TGA	Ala	CII	11:	Thre
Val	Leu	Lys	Gly	Tyr	vaı	ren	Giu	GIY	1111	reu	1111	VIG	314	Lys	Thr>
530			540			55	50		9	560			570		
•		•	•		•		•	•		•		•	•	•	•
ACA	TTG	GTG	GTT	AAA	GAA	GGA	ACT	GTT	ACT	TTA	AGC	AAA	AAT	ATT.	TCA
TGT	AAC	CAC	CAA	TTT	CTT	CCT	TGA	CAA	TGA	AAT	TCG	TTT	TTA	AAT.	AGT
Thr	Leu	.Val	Val	Lys	Glu	Gly	Thr	Val	Thr	Leu	Ser	Lys	Asn	Ile	Ser>
51	во		!	590			600			6	10		•	520	
		_				_					•	•			
	•	•	CAA	• •	ጥሮአ	CTT.	GE A	$-\tau$	* מממ	GAC	* ACT	GAC	AGT	AGT	CCT
ааа	TCT	GGG	GAA	GTT	TCA	GTT	GAA CTT	CTT	AAT	GAC CTG	ACT TGA	GAC CTG	AGT TCA	AGT TCA	GCT CGA
AAA TTT	AGA	CCC	CTT	CAA	AGT	CAA	CTT	GAA	TTA	CTG	TGA	CTG	TCA	TCA	CGA
AAA TTT	AGA	CCC	CTT	CAA	AGT	CAA	CTT	GAA	TTA	CTG	TGA	CTG	TCA	TCA	GCT CGA Ala>
AAA TTT	AGA	CCC	CTT	CAA Val	AGT	CAA	CTT Glu	GAA	TTA	CTG	TGA	CTG	TCA	TCA Ser	CGA
AAA TTT Lys	AGA Ser 630	CCC	CTT Glu	CAA Val	AGT Ser 40	CAA Val	CTT	GAA Leu 650	TTA Asn	Asp	TGA Thr 660	CTG Asp	TCA Ser	TCA Ser	CGA Ala>
AAA TTT Lys	AGA Ser 630	CCC Gly	CTT Glu	CAA Val 6	AGT Ser 40 • GCA	CAA Val	CTT Glu TGG	GAA Leu 650 AAT	TTA Asn GAC	Asp	TGA Thr 660	ASP AGC	TCA Ser	TCA Ser 67	CGA Ala> 70 • ACA
AAA TTT Lys GCT CGA	AGA Ser 630 ACT TGA	CCC Gly	CTT Glu AAA TTT	CAA Val 6 ACT TGA	AGT Ser 40 • GCA CGT	CAA Val GCT CGA	Glu TGG ACC	GAA Leu 650 AAT TTA	TTA Asn GAC CTG	ASP AGT TCA	TGA Thr 660 ACT TGA	ASP AGC TCG	TCA Ser ACT TGA	TCA Ser 61 TTA AAT	CGA Ala> 70 ACA TGT
AAA TTT Lys GCT CGA	AGA Ser 630 ACT TGA	CCC Gly	CTT Glu AAA TTT	CAA Val 6 ACT TGA	AGT Ser 40 • GCA CGT	CAA Val GCT CGA	Glu TGG ACC	GAA Leu 650 AAT TTA	TTA Asn GAC CTG	ASP AGT TCA	TGA Thr 660 ACT TGA	ASP AGC TCG	TCA Ser ACT TGA	TCA Ser 61 TTA AAT	CGA Ala> 70 • ACA
AAA TTT Lys GCT CGA	AGA Ser 630 ACT TGA	CCC Gly	CTT Glu AAA TTT	CAA Val 6 ACT TGA	AGT Ser 40 • GCA CGT	CAA Val GCT CGA Ala	Glu TGG ACC	GAA Leu 650 AAT TTA Asn	TTA Asn GAC CTG	ASP AGT TCA	TGA Thr 660 ACT TGA	ASP AGC TCG	TCA Ser ACT TGA	TCA Ser 61 TTA AAT	CGA Ala> 70 ACA TGT
AAA TTT Lys GCT CGA Ala	AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys	CTT Glu AAA TTT Lys	CAA Val 6 ACT TGA Thr	AGT Ser 40 • GCA CGT Ala 690	CAA Val GCT CGA Ala	TGG ACC	GAA Leu 650 AAT TTA Asn	GAC CTG Asp	ASP AGT TCA Ser	TGA Thr 660 ACT TGA Thr	AGC TCG Ser	Ser ACT TGA Thr	TCA Ser 61 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr>
AAA TTT Lys GCT CGA Ala	AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTI Lys 680	CTT Glu AAA TTT Lys	CAA Val 6 ACT TGA Thr	AGT Ser 40 • GCA CGT Ala 690	CAA Val GCT CGA Ala	TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7	GAC CTG Asp	CTG Asp AGT TCA Ser	TGA Thr 660 ACT TGA Thr	AGC TCG Ser	TCA Ser ACT TGA Thr	TCA Ser 61 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT
AAA TTT Lys GCT CGA Ala ATT	AGA Ser 630 ACT TGA Thr	AAA TTT Lys 680	CTT Glu AAA TTT Lys	CAA Val  6 ACT TGA Thr  AGC TCG	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala	TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7	GAC CTG Asp	CTG Asp AGT TCA Ser	TGA Thr 660 ACT TGA Thr CGCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	AGC TCG Ser	TCA Ser ACT TGA Thr	TCA Ser 61 TTA AAT Leu ACA	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA
AAA TTT Lys GCT CGA Ala ATT	AGA Ser 630 ACT TGA Thr	AAA TTT Lys 680	CTT Glu AAA TTT Lys	CAA Val  6 ACT TGA Thr  AGC TCG	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala	TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7	GAC CTG Asp	CTG Asp AGT TCA Ser	TGA Thr 660 ACT TGA Thr CGCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	AGC TCG Ser	TCA Ser ACT TGA Thr	TCA Ser 61 TTA AAT Leu ACA	CGA Ala> 70 ACA TGT Thr> 720 GAT
AAA TTT Lys GCT CGA Ala ATT	AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTI Lys 680 CGA CGA	CTT Glu AAA TTT Lys	CAA Val  6 ACT TGA Thr  AGC TCG	AGT Ser 40 • GCA CGT Ala 690 • AAA TTT Lys	CAA Val GCT CGA Ala	TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7	GAC CTG Asp	AGT AGT TCA Ser AAAO	TGA Thr 660 ACT TGA Thr CGCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	AGC TCG Ser	TCA Ser ACT TGA Thr	TCA Ser 61 TTA AAT Leu ACA	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA
AAA TTT Lys GCT CGA Ala ATT TAA	AGA Ser  630  ACT TGA Thr  AGT TCA Ser	AAA TTT Lys 680 CGA	CTT Glu AAA TTT Lys GAC CTG AST	CAA Val 6 ACT TGA Thr : AGC : TCG	AGT Ser 40 • GCA CGT Ala 690 • AAA TTT Lys	GCT CGA Ala AAA TTI Lys	TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7 AAA TTI Lys	GAC CTG Asp 00 GAT CTA Asp	AGT TCA Ser	TGA Thr 660 ACT TGA Thr CCAC	AGC TCG Ser 710 . TTC AAG Phe	ACT TGA Thr TTA AAT Leu 60	TCA Ser 67 TTA AAT Leu ACA TGT Thr	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA Asp>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	AGA Ser 630 ACT TGA Thr AGT TCA Ser	AAA TTT Lys 680 CGA CGA	CTT Glu AAA TTT Lys CTG ACTG	CAA Val  6 ACT TGA Thr  AGC TCG TCG	AGT Ser 40 GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT Lys 740	TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7 AAA TTI Lys	GAC CTG Asp 00 GAT CTA Asp	A GC	TGA Thr 660 ACT TGA Thr CCAC	AGC TCG Ser 710 AGC Phe	TCA Ser  ACT TGA Thr  TTA AAI Leu 60 .	TCA Ser  67  TTA AAT Leu  ACA TGT Thr	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA Asp>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	AGA Ser 630 ACT TGA Thr AGT TCA Ser	AAA TTT Lys 680 CGA CGA ATTT	CTT Glu AAA TTT Lys CTG A CTG	CAA Val  6 ACT TGA Thr  AGC TCG TCG TCG	AGT Ser 40 GCA CGT Ala 690 AAA TTT Lys	CAA Val  GCT CGA Ala  AAA TTT Lys 740 . CAA . GTT	TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7 AAA TTI Lys	GAC GAC GAT	CTG ASP AGT TCA Ser AAA AAA AAAA AAAA AAAAA AAAAAAAAAA	TGA Thr 660 ACT TGA Thr CCAC	AGC TCG Ser 710 TTC AAG Phe	TCA Ser  ACT TGA Thr  TTA AAT Leu 60 .	TCA Ser  6° TTA AAT Leu ACA TGT Thr	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA Asp>

FIGURE 29 (2 of 3)

B-31 OSP A/ B-31 OSP B FUSION

770 780 790 800 810

GGA TCA GCA AGT GAA ATT AAA AAT CTT TCA GAG CTT AAA AAC GCT TTA
CCT AGT CGT TCA CTT TAA TTT TTA GAA AGT CTC GAA TTT TTG CGA AAT
Gly Ser Ala Ser Glu Ile Lys Asn Leu Ser Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys \*\*\*>

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### B-31 OSP A/ B-31 OSP B / B-31 OSP C FUSION

nce Range: 1 to 1401

30 20 10 ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TIT TIT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala> 80 70 60 50 TGT AAG CAA AAT GTT AGC AGC CTT GAC GAG AAA-AAC AGC GTT TCA GTA ACA TTC GTT TTA CAA TCG TCG GAA CTG CTC TTT TTG TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val> 130 120 110 GAT TTG CCT GGT GAA ATG AAA GTT CTT GTA AGC AAA GAA AAA AAC AAA CTA AAC GGA CCA CTT TAC TTT CAA GAA CAT TCG TTT CTT TTT TTG TTT Asp Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asn Lys> 180 170 160 150 GAC GGC AAG TAC GAT CTA ATT GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCG TTC ATG CTA GAT TAA CGT TGT CAT CTG TTC GAA CTC GAA TTT Asp Gly Lys Tyr Asp Leu Ile Ala Thr Val Asp Lys Leu Glu Leu Lys> 220 210 200 GGA ACT TCT GAT AAA AAC AAT GGA TCT GGA GTA CTT GAA GGC GTA AAA CCT TGA AGA CTA TTT TTG TTA CCT AGA CCT CAT GAA CTT CCG CAT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Val Leu Glu Gly Val Lys> 280 270 260 GCT GAC AAA AGT AAA GTA AAA TTA ACA ATT TCT GAC GAT CTA GGT CAA CGA CTG TTT TCA TTT CAT TTT AAT TGT TAA AGA CTG CTA GAT CCA GTT Ala Asp Lys Ser Lys Val Lys Leu Thr Ile Ser Asp Asp Leu Gly Gln> 330 320 310 300 290 ACC ACA CTT GAA GTT TTC AAA GAA GAT GGC AAA ACA CTA GTA TCA AAA TGG TGT GAA CTT CAA AAG TTT CTT CTA CCG TTT TGT GAT CAT AGT TTT Thr Thr Leu Glu Val Phe Lys Glu Asp Gly Lys Thr Leu Val Ser Lys> 370 360 340 350 AAA GTA ACT TCC AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAT GAA TIT CAT TGA AGG TIT CTG TTC AGT AGT TGT CTT TTT AAG TTA CTT

FIGURE 30 (1 of 4)

Lys Val Thr Ser Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu>

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# B-31 OAP A/ B-31 OSP B / B-31 OSPC FUSION

		40			4	10			420			43	9
390	٠			•		•		•	•		•		•
AAA GGT GAA	ата	тст	GAA	AAA	ATA	ATA	ACA	AGA	GCA	GAC	GGA	ACC	AGA
TTT CCA CTT Lys Gly Glu	Val	Ser	Glu	Lys	Ile	Ile	Thr	Arg	Ala	Asp	Gly	Thr	Arg>
Lys GI, CI-										_			
440			450			4	60	_	4	170			480
• •		•	•		•		•	~~	~~1			222	CSC
CTT GAA TAC	: ACA	GGA	ATT	AAA	AGC	GAT	GGA	TCT	ADD TOT	AAA TTT	CCI	WW.	CTC
		~~~	~~~	dalal.	717 (6	LIA		AUA	~~ 1				
GAA CTT ATC	Thr	Gly	Ile	Lys	Ser	Asp	GIA	ser	GIÀ	rys	WIG	Lys	010>
				500			510				20		
	190			•		•	•		•		•	•	
GTT TTA AA		ጥልጥ	GTT	СТТ	GAA	GGA	ACT	СТА	ACT	GCT	GAA	AAA	ACA
			~~~		7 1 1		1130		100				
CAA AAT TT Val Leu Ly	e CJA	Tvr	Val	Leu	Glu	Gly	Thr	Lev	Thr	Ala	Glu	Lys	Thr>
val Leu Ly	5 017	-,-											
530	540	)		5	50			560		_	570		_
_	•	,	•		•	•	•			•	•		
ACA TTG GT	G GT7	IAA 1	<b>GAA</b>	GGZ	A ACT	GT	L YC1	עדדי :	AGC	: AA	, www	WII	1CA
			_~~~	, ,	r TGJ	L CA	10/	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	1 1	, ,,,			
TGT AAC CA	1 Va.	l Lys	s Glu	L Gly	נתד י	r Va.	I Thi	Lei	1 261	L. L.Y:	> W21	110	
													,
500					60				610			620	,
580		590		•	60	0	•	,	610	,	•	620	
•	•	590	m	•	60) CA	0 • • CT	• T AA'	r GA	610 •	r GA	• C AG	620 •	r GCT
AAA TCT GO	• GG GA	590 • A GT	r rcz	· A GT	60 T GA	D • A CT	T AA' A TT.	r ga	610 • C ACT	T GA	• C AGI	620 T AGT	r GCT
AAA TCT GO	• GG GA	590 • A GT	r rcz	· A GT	60 T GA	D • A CT	T AA' A TT.	r ga	610 • C ACT	T GA	• C AGI	620 T AGT	r GCT
•	• GG GA	590 A GT T CA u Va	T TCA A AGI 1 Sei	· A GT	60 T GA	O A CT T GA u Le	T AA' A TT. u As:	r ga	610 C AC G TG p Th	T GA A CT I As	• C AGI	620 • AGT A TCI c Se:	r GCT A CGA r Ala>
AAA TCT GO	• GG GA	590 A GT T CA u Va	r rcz	· A GT	60 T GA	D • A CT	T AA' A TT. u As:	r ga	610 • C ACT	T GA A CT I As	• C AGI	620 • AGT A TCI c Se:	r GCT
AAA TCT GC TTT AGA CC Lys Ser G	G GA CC CT ly G1	590 A GT T CA u Va	T TCA A AG 1 Se:	A GT T CA r Va	60 T GA A CT 1 G1	A CT T GA u Le	T AA' A TT. u As:	T GA A CT n As	610 C ACT G TG P Th	T GA A CT I As	C AGT G TCI p Set	620 • AGT A TCI c Se:	GCT A CGA r Ala>
AAA TCT GC TTT AGA CC Lys Ser G	GG GA	590 A GT T CA u Va	T TCA A AG 1 Se:	A GT T CA r Va	600 T GA A CT 1 G1	A CT GA Le	T AA'A TT. U AS:	T GA A CT n As	610 C ACT G TG. p Th. 66	T GA A CT T AS	C AGT G TCI p Set	620 A TCA T Ser	GCT A CGA C Ala>
AAA TCT GC TTT AGA CC Lys Ser G: 630	GG GA	590 A GT T CA U Va	T TCA A AGT 1 Sec 640	A GT CA r Va A GC	600 T GA A CT 1 G1	O A CT GA Le G G AA	T AA'A TT. U AS:	T GA A CT n As	610 C ACT G TG D Th  66 TACT TACT TACT TACT TACT TACT TACT	T GA A CT I As 0 T AG	E AG	620  A TCA  T Se:	r GCT A CGA r Ala> 670 A ACA T TGT
AAA TCT GC TTT AGA CC Lys Ser G	GG GA	590 A GT T CA U Va	T TCA A AGT 1 Sec 640	A GT CA r Va A GC	600 T GA A CT 1 G1	O A CT GA Le G G AA	T AA'A TT. U AS:	T GA A CT n As	610 C ACT G TG D Th  66 TACT TACT TACT TACT TACT TACT TACT	T GA A CT I As 0 T AG	E AG	620  A TCA  T Se:	r GCT A CGA r Ala> 670 A ACA T TGT
AAA TCT GC TTT AGA CC Lys Ser G:  630  GCT ACT A CGA TGA T Ala Thr L	GG GA CC CT LY G1 AA AA ATT TI YS LY	590 A GT T CA U Va	T TC/A AG' 1 Se: 640 T GC A CG	A GT CA r Va A GC T CG a Al	600 T GA A CT 1 G1	O A CT GA Le G G AA	T AA'A TT. U AS:	T GA A CT n As	610 C ACT G TG D Th  66 TACT TACT TACT TACT TACT TACT TACT	T GA A CT I As 0 T AG	C AGE G TCI P See	620  A TCA  T Se:	r GCT A CGA r Ala> 670 A ACA T TGT
AAA TCT GC TTT AGA CC Lys Ser G:  630 GCT ACT A CGA TGA T Ala Thr L	GG GA CC CT LY G1 AA AA TT TI YS LY	590 A GT T CA U Va A AC T TG	T TCA A AGT 1 Se: 640 T GC A CG AT A1	A GTT CA	GOO T GA A CT 1 G1 T TO SA AC	A CT GA Le 650	T AA'A TT GA	T GA A CT n As C AG C AG G TC	610 C AC G TG p Th 66 ct AC CA TG	T GA A CT T AS T AG A TC	C AGT G TCI p Set C ACT G TG	620 A TCJ C Ser T TT A AA	r GCT A CGA r Ala> 670 A ACA T TGT u Thr>
AAA TCT GC TTT AGA CC Lys Ser G: 630 GCT ACT A CGA TGA T Ala Thr L	GG GA CC CT LY G1 AA AA TT TI YS LY	590 A GT T CA U Va A AC T TG	T TCA A AG 1 Se: 640 ET GC EA CG EA CG	A GT Va	GOO T GA A CT 1 G1 T TC GA AC	A CT GA Le GA A CT T A CT A CT A CT A CT A CT A CT	T AA' A TT U AS: AT GA TA CT SIN AS	T GAA CT A A CT A A CT A CT A CT A CT A	610 C AC G TG P Th 66 ST AC CA TG	T GAA CT AS TO AS	C AGT G TCI p Set C ACT G TG	620 T AGTA TCA T TTA A AA T Le	r GCT A CGA r Ala> 670 A ACA T TGT u Thr> 720
AAA TCT GC TTT AGA CC Lys Ser G: 630 GCT ACT A CGA TGA T Ala Thr L	GG GA CC CT LY G1 AA AA TT TI YS LY	590 A GT T CA U Va A AC A	T TCA A AG 1 Se: 640 T GC A CG A CG A A1	A GCT CG a Al	GOO T GA A CT 1 G1 T TO A AC	A CT GA GE GA A CC TT A CC A CC TT A CC A CC A CC	T AA' A TT U AS AT GA FA CT SIN AS	T GA A CT A AS C AG C TC	610 C ACT G TG. P Th: 66 CT ACC CA TG. CT Th: 1G GT ACC. CI	T GAA A CT T AG A TO T AG	C AGE C ACE C ACE C TO C TO AG AG	620 T AGT A TCA T TT A AA T Le	F GCT A CGA F Ala> 670 A ACA T TGT U Thr> 720 CA GAT GT CTA
AAA TCT GC TTT AGA CC Lys Ser G: 630 GCT ACT A CGA TGA T Ala Thr L	GG GA CC CT LY G1 AA AA TT TI YS LY	590 A GT T CA U Va A AC A	T TCA A AG 1 Se: 640 T GC A CG A CG A A1	A GCT CG a Al	GOO T GA A CT 1 G1 T TO A AC	A CT GA GE GA A CC TT A CC A CC TT A CC A CC A CC	T AA' A TT U AS AT GA FA CT SIN AS	T GA A CT A AS C AG C TC	610 C ACT G TG. P Th: 66 CT ACC CA TG. CT Th: 1G GT ACC. CI	T GAA A CT T AG A TO T AG	C AGE C ACE C ACE C TO C TO AG AG	620 T AGT A TCA T TT A AA T Le	F GCT A CGA F Ala> 670 A ACA T TGT U Thr> 720 CA GAT GT CTA
AAA TCT GC TTT AGA CC Lys Ser G: 630 GCT ACT A CGA TGA T Ala Thr L	GG GA CC CT LY G1 AA AA TT TI YS LY	590 A GT T CA U Va A AC A	T TCA A AG 1 Se: 640 T GC A CG A CG A A1	A GTT CA A GC T CA A GC T CG A Al	600 T GA A CT 1 G1 T TO AA AC	A CT GA GE GA A CC TT A CC A CC TT A CC A CC A CC	T AA' A TT U AS: AT GA TA CT SIN AS: 700 AA GI TT CT	T GA A CT D AS C AG G TC C AG T TA AT T TA A SSP L	610 C ACT G TG. P Th: 66 CT ACC CA TG. CT Th: 1G GT ACC. CI	T GAA A CT T AG A TO T AG	C AGE G TCI P See C AC G TG TT TT AG AI he Le	620 T AGT A TCA T TT A AA T Le	F GCT A CGA F Ala> 670 A ACA T TGT U Thr> 720 CA GAT GT CTA
AAA TCT GC TTT AGA CC Lys Ser G: 630 GCT ACT A CGA TGA T Ala Thr L	GG GA CC CT LY G1 AA AA TT TI YS LY	590 A GT T CA U Va A AC AC AC SSP SS	T TCA A AG 1 Se: 640 T GC A CG A CG A A1	A GCT CG a Al	600 T GA A CT 1 G1 T TO AA AC	A CT GA GE GA A CC TT A CC A CC TT A CC A CC A CC	T AA' A TT U AS: AT GA TA CT SIN AS: 700 AA GI TT CT	T GA A CT A AS C AG C TC	610 C ACT G TG. P Th: 66 CT ACC CA TG. CT Th: 1G GT ACC. CI	T GAA A CT T AG A TO T AG	C AGE C ACE C ACE C TO C TO AG AG	620 T AGT A TCA T TT A AA T Le	F GCT A CGA F Ala> 670 A ACA T TGT U Thr> 720 CA GAT GT CTA
AAA TCT GC TTT AGA CC Lys Ser G  630  GCT ACT A CGA TGA T Ala Thr L  68  ATT AGT G TAA TCA C Ile Ser A	AA AA TT TI YS Ly CGA C	590 A GT T CA U Va A AC T TG T	T TCA A AG' 1 Se: 640 T GC A CG AT A1 69 GC AF GC AF	A GT CA T CA A GC T CG A Al O IA Al TT T 74	GOO T GA A CT 1 G1 T TO AA AI TT TO YS T	650 AA CT T GA GG AA CC TT A SC TT A T CT A T CT A T	T AA'A TT. U AS: AT GA TA CT SIN AS 700 AA GI TT C' ys A:	T GA A CT A A CT C AG C TC C F Se AT T AT T A A SSP L	610 C AC G TG p Th 66 ET AC EX TG EX Th	T GA A CT T AS O T AG T AG T TAG T T TAG T T T T T T T T T T T T T T T T T T T	C AGE OF SEE  OF ACT OF TO OF OF TO	620  T AGT A TCI T TT A AA I Le	GCT A CGA C Ala> 670 A ACA T TGT U Thr> 720 CA GAT GT CTA Dr Asp>
AAA TCT GC TTT AGA CC Lys Ser G:  630  GCT ACT A CGA TGA T Ala Thr L  68  ATT AGT G TAA TCA C Ile Ser F	AA AA TT TI YS Ly CGA C	590 A GT T CA U Va A AC T TG TS TH	T TCA A AG' 1 Se: 640 T GC A CG A A A GC AP er Ly	A GCT CG A AI	GOO T GA A CT T TO SA AC T TO YS T	O A CT T GA A CC A	T AA' A TT. U AS: IT GA TA CT	T GA A CT D AS C AG C AG C T C AG C T C AG C T C AG	610 C ACT G TG G TG CT ACC CT	T GAA A CT AS T AG AT T AG TAG TAG TAG TAG TAG TAG TAG TAG TAG T	C AGE C AGE C AGE C AGE C AGE C Th	620 T AGT A TCI T TTT A AA I Le	F GCT A CGA F Ala> 670 A ACA T TGT U Thr> 720 CA GAT GT CTA DT ASP>
AAA TCT GC TTT AGA CC Lys Ser G  630  GCT ACT A CGA TGA T Ala Thr L  68  ATT AGT G TAA TCA C Ile Ser A	AA AA TT TI YS LY CGA C T30 ATT A	A GT T CA U VA	T TCA A AG' 1 Se: 640 T GC A CG A CG T A1 er Ly	A GCT Va A GCCT A AI O AI O	GOO T GA A CT T TO SA AC TT TO YS T	A CT	T AA' A TT. U AS: AT GA TA CT	T GA A CT n As C AG G TC AT T TA A A SSP L CAG GT C	610 C ACT G TG D Th  66 CT ACT CA TG ACT CU CCT G CGA C	T GAA A CT T AS T AG A TO T AG T AG AC AA AC T T	C AGE C AGE C AGE C AGE C Th	620  T AGT A TCJ T TTT A AAA T Le  CA ACC CT TCC CG G	F GCT A CGA F Ala> 670 A ACA T TGT U Thr> 720 CA GAT CTA DI ASP> IA GAA AT CTT

FIGURE 30 (2 of 4)

#### .B-31 OSP A/ B-31 OSP B / B-31 OSP C FUSION

770			780			79	0		8	00			810		
•		•	•		•		•	•		•		•	•		•
				GAA											
				CTT											
Gly	Ser	Ala	Ser	Glu	Ile	Lys	Asn	Leu	Ser	Glu	Leu	Lys	ÀS.	Ala	Leu>
82	20		8	30			840			85	50		9	550	
	•	•		•		•	•		•		•	•		•	
				TAA											
				ATT											
Lys	Met	Ala	Asn	Asn	Ser	Gly	Lys	Asp	GŢĀ	ASD.	Thr	Ser	Ala	Asn	Ser>
	870			88	30		8	90			900	•		91	. 3
•	•		•		•	*		•		•	•		•		•
				GTT											
				CAA											
Ala	Asp	Glu	Ser	Val	Lys	Gly	Pro	Asn	Leu	Thr	Glu	Ile	Ser	Lys	Lys>
	. 9	920			930			94	0		9	950			960
•		•		•			*		•			•		•	•
				AAT											
				TTA											
11e	Inr	ASP	Ser	ASD	AIG	vai	Leu	Leu	WIG	val	Lys	GIG	vaı	GIU	Ala>
	•	9	70	•	!	980		•	990		•	100	00	•	
TTG	• CTG		•	+ ATA		•	тта	• GCT	•	AAA	• GCT		•		AAA
		TCA	TCT	- ATA TAT	GAT	• GAA			GCT			ATT	• GGT		
AAC	GAC	TCA AGT	TCT AGA	TAT	GAT CTA	GAA CTT	TAA	CGA	GCT CGA	TTT	CGA	TTA AAT	• GGT CCA	TTT	
AAC	GAC	TCA AGT Ser	TCT AGA	TAT	GAT CTA	GAA CTT	TAA Ile	CGA	GCT CGA Ala	TTT	CGA	ATT TAA Ile	• GGT CCA	TTT	TTT
AAC Leu	GAC	TCA AGT Ser	TCT AGA Ser	TAT	GAT CTA	GAA CTT Glu	TAA Ile	CGA	GCT CGA Ala	TTT Lys	CGA	ATT TAA Ile	GGT CCA Gly	TTT	TTT
AAC Leu 1010 * ATA	GAC Leu CAC	TCA AGT Ser	TCT AGA Ser 1020	TAT Ile	GAT CTA Asp	GAA CTT Glu	TAA Ile 30 • GAT	CGA Ala	GCT CGA Ala 1	TTT Lys 040 TAT	CGA Ala AAT	ATT TAA Ile CAC	GGT CCA Gly 1050	TTT Lys GGA	TTT Lys> • TCA
AAC Leu 1010 * ATA TAT	GAC Leu CAC GTG	TCA AGT Ser • CAA	TCT AGA Ser 1020 AAT	TAT Ile AAT TTA	GAT CTA Asp GGT CCA	GAA CTT Glu 10: TTG AAC	TAA Ile 30 GAT CTA	CGA Ala ACC TGG	GCT CGA Ala 1 GAA CTT	TTT Lys 040 * TAT ATA	CGA Ala AAT TTA	ATT TAA Ile CAC GTG	GGT CCA Gly 1050 AAT TTA	TTT Lys GGA CCT	TTT Lys> TCA AGT
AAC Leu 1010 * ATA TAT	GAC Leu CAC GTG	TCA AGT Ser • CAA	TCT AGA Ser 1020 AAT	TAT Ile AAT TTA	GAT CTA Asp GGT CCA	GAA CTT Glu 10: TTG AAC	TAA Ile 30 GAT CTA	CGA Ala ACC TGG	GCT CGA Ala 1 GAA CTT	TTT Lys 040 * TAT ATA	CGA Ala AAT TTA	ATT TAA Ile CAC GTG	GGT CCA Gly 1050 AAT TTA	TTT Lys GGA CCT	TTT Lys> • TCA
AAC Leu 1010 * ATA TAT	GAC Leu CAC GTG His	TCA AGT Ser • CAA	TCT AGA Ser 1020 AAT TTA Asn	TAT Ile AAT TTA	GAT CTA Asp GGT CCA	GAA CTT Glu 10: TTG AAC Leu	TAA Ile 30 GAT CTA	CGA Ala ACC TGG	GCT CGA Ala 1 GAA CTT	TTT Lys 040 * TAT ATA	CGA Ala AAT TTA Asn	ATT TAA Ile CAC GTG	GGT CCA Gly 1050 AAT TTA Asn	TTT Lys GGA CCT	TTT Lys> TCA AGT
AAC Leu 1010 ATA TAT Ile	GAC Leu CAC GTG His	TCA AGT Ser CAA GTT Gln	TCT AGA Ser 1020 AAT TTA Asn	TAT Ile AAT TTA Asn 070	GAT CTA Asp GGT CCA Gly	GAA CTT Glu 10: TTG AAC Leu	TAA Ile 30 GAT CTA ASP	CGA Ala ACC TGG Thr	GCT CGA Ala 1 GAA CTT Glu	TTT Lys 040 TAT ATA Tyr	AAT TTA ASD	ATT TAA Ile CAC GTG His	GGT CCA Gly 1050 AAT TTA Asn	GGA CCT Gly	TTT Lys> TCA AGT Ser>
AAC Leu 1010 ATA TAT Ile 10	GAC Leu CAC GTG His	TCA AGT Ser CAA GTT Gln	TCT AGA Ser 1020 AAT TTA Asn	TAT Ile  AAT TTA Asn  O70  CGT	GAT CTA Asp GGT CCA Gly	GAA CTT Glu 10: TTG AAC Leu	TAA Ile 30 GAT CTA ASP 1080	CGA Ala ACC TGG Thr	GCT CGA Ala 1 GAA CTT Glu	TTT Lys 040 TAT ATA Tyr 10	AAT TTA ASD	ATT TAA Ile CAC GTG His	GGT CCA Gly 1050 AAT TTA Asn	GGA CCT Gly	TTT Lys> TCA AGT Ser>
AAC Leu 1010 * ATA TAT Ile 10 TTG AAC	CAC GTG His	TCA AGT Ser CAA GTT Gln	TCT AGA Ser 1020 AAT TTA Asn 1 GGA CCT	TAT Ile AAT TTA Asn 070 CGT GCA	GAT CTA Asp GGT CCA Gly TAT	GAA CTT Glu 10: TTG AAC Leu	TAA Ile 30 GAT CTA ASP 1080 ATA TAT	CGA Ala ACC TGG Thr TCA AGT	GCT CGA Ala 1 GAA CTT Glu ACC TGG	TTT Lys 040 TAT ATA Tyr 10 CTA GAT	AAT TTA ASD  ATA TAT	ATT TAA Ile CAC GTG His	GGT CCA Gly 1050 AAT TTA Asn 1: CAA GTT	GGA CCT Gly 100	TTT Lys> TCA AGT Ser> TTA AAT
AAC Leu 1010 * ATA TAT Ile 10 TTG AAC	CAC GTG His	TCA AGT Ser CAA GTT Gln	TCT AGA Ser 1020 AAT TTA Asn 1 GGA CCT	TAT Ile AAT TTA Asn 070 CGT GCA	GAT CTA Asp GGT CCA Gly TAT	GAA CTT Glu 10: TTG AAC Leu	TAA Ile 30 GAT CTA ASP 1080 ATA TAT	CGA Ala ACC TGG Thr TCA AGT	GCT CGA Ala 1 GAA CTT Glu ACC TGG	TTT Lys 040 TAT ATA Tyr 10 CTA GAT	AAT TTA ASD  ATA TAT	ATT TAA Ile CAC GTG His	GGT CCA Gly 1050 AAT TTA Asn 1: CAA	GGA CCT Gly 100	TTT Lys> TCA AGT Ser>
AAC Leu 1010 * ATA TAT Ile 10 TTG AAC	CAC GTG His	TCA AGT Ser CAA GTT Gln GCG CGC Ala	TCT AGA Ser 1020 AAT TTA Asn 1 GGA CCT	TAT Ile AAT TTA Asn 070 CGT GCA	GAT CTA Asp GGT CCA Gly TAT ATA Tyr	GAA CTT Glu 10: TTG AAC Leu	TAA Ile 30 GAT CTA ASP 1080 ATA TAT Ile	CGA Ala ACC TGG Thr TCA AGT	GCT CGA Ala 1 GAA CTT Glu ACC TGG	TTT Lys 040 TAT ATA Tyr 10 CTA GAT Leu	AAT TTA ASD  ATA TAT	ATT TAA Ile CAC GTG His	GGT CCA Gly 1050 AAT TTA Asn 1: CAA	GGA CCT Gly 100	TTT Lys> TCA AGT Ser> TTA AAT Leu>
AAC Leu 1010 * ATA TAT Ile 10 TTG AAC Leu	CAC GTG His 60 TTA AAT Leu	TCA AGT Ser CAA GTT Gln GCG CGC Ala	TCT AGA Ser 1020 AAT TTA Asn 1 GGA CCT Gly	TAT Ile AAT TTA ASD 070 CGT GCA Arg	GAT CTA Asp GGT CCA Gly TAT ATA Tyr	GAA CTT Glu 10: TTG AAC Leu	TAA Ile 30 GAT CTA ASP 1080 ATA TAT Ile	CGA Ala ACC TGG Thr TCA AGT Ser	GCT CGA Ala 1 GAA CTT Glu ACC TGG Thr	TTT Lys 040 TAT ATA Tyr 10 CTA GAT Leu	AAT TTA ASD  O ATA TAT Ile	ATT TAA Ile CAC GTG His	GGT CCA Gly 1050 AAT TTA Asn 1 CAA GTT Gln	GGA CCT Gly 100 AAA TTT Lys	TTT Lys> TCA AGT Ser> TTA AAT Leu>
AAC Leu 1010 ATA TAT Ile 10 TTG AAC Leu GAT	CAC GTG His 60 TTA AAT Leu	TCA AGT Ser CAA GTT Gln GCG CGC Ala	TCT AGA Ser 1020 AAT TTA Asn 1 GGA CCT Gly	TAT Ile AAT TTA ASD O70 CGT GCA Arg	GAT CTA Asp GGT CCA Gly TAT ATA Tyr	GAA CTT Glu 10: TTG AAC Leu * GCA CGT Ala	TAA Ile 30 GAT CTA ASP 1080 ATA TAT Ile	ACC TGG Thr  TCA AGT Ser  130	GCT CGA Ala 1 GAA CTT Glu ACC TGG Thr	TTT Lys 040 TAT ATA Tyr 10 CTA GAT Leu	AAT TTA ASD ATA TAT 11e	ATT TAA Ile  CAC GTG His  AAA TTT Lys	GGT CCA Gly 1050 AAT TTA Asn CAA GTT GIn	GGA CCT Gly 100 AAA TTT Lys	TTT Lys> TCA AGT Ser> TTA AAT Leu> S0 AAG
AAC Leu 1010 ATA TAT Ile 10 TTG AAC Leu GAT CTA	CAC GTG His 60 TTA AAT Leu 1110 GGA	TCA AGT Ser CAA GTT Gln GCG CGC Ala	TCT AGA Ser 1020 AAT TTA Asn 1 GGA CCT Gly	TAT Ile  AAT TTA Asn  O70  CGT GCA Arg  11  AAT TTA	GAT CTA Asp GGT CCA Gly TAT ATA Tyr	GAA CTT Glu 10: TTG AAC Leu * GCA CGT Ala	TAA Ile 30 GAT CTA ASP 1080 ATA TAT Ile 1 TTA	ACC TGG Thr  TCA AGT Ser  130 AAG TTC	GCT CGA Ala 1 GAA CTT Glu ACC TGG Thr	TTT Lys 040 TAT ATA Tyr 10 CTA GAT Leu	AAT TTA ASD ATA TAT Ile	ATT TAA Ile CAC GTG His AAA TTT Lys	GGT CCA Gly 1050 AAT TTA ASn CAA GTT Gln GCG CGC	GGA CCT Gly 100 AAA TTT Lys 11:	TTT Lys> TCA AGT Ser> TTA AAT Leu>

FIGURE 30 (3 of 4)

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## B-31 OSP A / B-31 OSP B/ B-31 OSP C FUSION

1190 1180 1170 1160 AAA TGT TCT GAA ACA TTT ACT AAT AAA TTA AAA GCA AAA CAC ACA GAT TTT ACA AGA CTT TGT AAA TGA TTA TTT AAT TTT CGT TTT GTG TGT CTA Lys Cys Ser Glu Thr Phe Thr Asn Lys Leu Lys Ala Lys His Thr Asp> 1240 1230 1220 1210 CTT GGT AAA GAA GGT GTT ACT GAT GCT GAT GCA AAA GAA GCC ATT TTA GAA CCA TTT CTT CCA CAA TGA CTA CGA CTA CGT TTT CTT CGG TAA AAT Leu Gly Lys Glu Gly Val Thr Asp Ala Asp Ala Lys Glu Ala Ile Leu> 1290 1280 1270 1260 1250 • AAA ACA AAT GGT ACT AAA ACT AAA GGT GCT GAA GAA CTT GGA AAA TTA TTT TGT TTA CCA TGA TTT TGA TTT CCA CGA CTT CTT GAA CCT TTT AAT Lys Thr Asn Gly Thr Lys Thr Lys Gly Ala Glu Glu Leu Gly Lys Leu> 1320 1330 1310 TTT GAA TCA GTA GAG GTC TTG TCA AAA GCA GCT AAA GAG ATG CTT GCT AAA CTT AGT CAT CTC CAG AAC AGT TTT CGT CGA TTT CTC TAC GAA CGA Phe Glu Ser Val Glu Val Leu Ser Lys Ala Ala Lys Glu Met Leu Ala> 1380 1370 1360 1350 • . • . . AAT TCA GTT AAA GAG CTT ACA AGC CCT GTT GTG GCA GAA AGT CCA AAA TTA AGT CAA TTT CTC GAA TGT TCG GGA CAA CAC CGT CTT TCA GGT TTT Asn Ser Val Lys Glu Leu Thr Ser Pro Val Val Ala Glu Ser Pro Lys>

1400

AAA CCT TAA TTT GGA ATT Lys Pro \*\*\*>

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#### B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

		1	.0			20			30			4	0		
	•		•	•		•		•	•		•		•	•	
ATG	AAA	AAG	AAT	ACA	TTA	AGT	GCG	ATA	TTA	ATG	ACT	ATT	TTT	TTA	TTT
TAC	TTT	TTC	TTA	TGT	AAT	TCA	CGC	TAT	AAT	TAC	TGA	AAT	AAA	TAA	AAA
Met	Lys	Lys	Asn	Thr	Leu	Ser	Ala	Ile	Leu	Met	Thr	Leu	Phe	Leu	Phe>
50			60			7	70			80			90		
•		•	•		•		•	•		•		•	•		•
ATA	TCT	TGT	AAT	TAA	TCA	GGG	AAA	GAT	GGG	TAA	ACA	TCT	GCA	TAA	TCT
TAT	AGA	ACA	TTA	TTA	AGT	CCC	TTT	CTA	CGC	TTA-	TGT	AGA	CGT	TTA	AGA ု
Ile	Ser	Cys	Asn	Asn	Ser	Gly	Lys	Asp	Gly	Asn	Thr	Ser	Ala	Asn	Ser>
10	0		1	.10			120			13	0		3	40	
	•	•		•		•	•		•		•	•		•	
		GAG													
CGA	CTA	CTC	AGA	CAA	TTT	CCC	GGA	TTA	GAA	TGT	CTT	TAT	TCA	TIT	ŢŢŢ.
Ala	Asp	Glu	Ser	Val	Lys	Gly	Pro	Asn	Leu	Thr	Glu	Ile	Ser	Ľys	Lys>
	150			16	0		1	170			180			19	0
•	•		•	-	•	•		•		•	•		•		•
ATT	ACG	GAT	TCT	AAT	GCG	GTT	TTA	CTT	GCT	GTG	AAA	GAG	GTT	GAA	GCG
TAA	TGC	CTA	AGA	TTA	CGC	CAA	AAT	GAA	CGA	CAC	TTT	CTC	CAA	CTT	CGC
Ile	Thr	Asp	Ser	Asn	Ala	Val	Leu	Leu	Ala	Val	Lys	Glu	Val	Glu	Ala>
		200			210			2:	20		2	230			240
•		•		• .	•		•		•	•		•		•	•
TTG	CTG	TCA	TCT	ATA	GAT	GAA	ATT	GCT	GCT	AAA	GCT	TTA	GGT	AAA	<del>አ</del> ኢት
AAC	GAC	AGT	AGA	TAT	CTA	CTT	TAA	CGA	CGA	TTT	CGA	TAA	CCA	TTT	TTT
Leu	Leu	Ser	Ser	Ile	Asp	Glu	Ile	Ala	Ala	Lys	Ala	Ile	Gly	Lys	Lys>
		2:	50		:	260			270			21	во		
	•		•	•		•		•	•		•		•	•	
ATA	CAC	CAA	AAT	AAT	GGT	TTG	GAT	ACC	GAA	TAT	AAT	CAC	TAA	GGA	TCA
		GTT													
Ile	His	Gln	Asn	Asn	Gly	Leu	Asp	Thr	Glu	ТУT	Asn	His	Asn	GIÀ	Ser>
290			300			3	10			320			330		
•		•	•		•		•	•		•		•	•		•
TTG	TTA	GCG	GGA	CGT	TAT	GCA	ATA	TCA	ACC	CTA	ATA	AAA	CAA	AAA	TTA
AAC	TAA	, CCC	CCT	GCA	ATA	CGI	TAT	AGT	TGG	GAT	TAT	ŢTT	GTT	TIT	TAA
Leu	Leu	Ala	Gly	Arg	Tyr	Ala	lle	Ser	Thr	Leu	lle	Lys	Gln	Lys	Leu>
3	40			350			360	)		3	70			380	
	•	•		•		•	•		•		•	•		•	
GAT	GGA	TTG	AAA	TAA	GAA	GGZ	ATT A	AAC	GAA	AAA .	. ATT	GAT	GCG	GCT	AAG
															TTC
Ast	Glv	, Leu	Lys	Asn	Glu	Gly	Lev	Lys	: Glu	ı Lys	: Ile	Asp	Ala	. Ala	Lys

## B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

3	90			40	0	•	4	10			420		_	43	ð
•	•	_ :_	•		•	•		•	mer a	*	CCN	**	CYC	1C2	CAT
T AAA	TOT	TCT	GAA	ACA TOT	1.1.1.	ACT.	ተጥ አ	ለለለ ጥጥጥ	TAA	ተተተ	CGT	TTT	GTG	TGT	CTA
Lys C	NCA NC	ROA	Glu	Thr	Phe	Thr	Asn	Lvs	Leu	Lys	Ala	Lys	His	Thr	Asp>
Lys	.y 3	JC1	014							•		•	-		•
	4	40			450			46	0		4	70			480
•		•		•	•		•		•	•		•		•	*
CTT (	GGT	AAA	GAA	GGT	GTT	ACT	GAT	GCT	GAT	GCA	AAA	GAA	GCC	ATT	TTA
GAA (	CCA	TTT	CIT	CCA	CAA	TGA	CTA	CGA	CIA	(CG1 1 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	Tue	CII	λla	TAN	· DII
Leu (	Gly	Lys	GIU	GIA	vai	inr	ASP	MIG	wah	VIG	Lys	GIU	A10	226	<b></b>
		Δ	90		5	00			510			52	0		
	•	7.	•	•		•		•	•		•		•	•	
AAA 2	ACA	AAT	GGT	ACT	AAA	ACT	AAA	GGT	GCT	GAA	GAA	CTT	GGA	ልልል	TTA
TTT	TGT	TTA	CCA	TGA	TTT	TGA	TTT	CCA	CGA	CTT	CTT	GAA	CCT	TTT	AAT
Ĺys '	Thr	Asn	Gly	Thr	Lys	Thr	Lys	Gly	Ala	Glu	Glu	Leu	Gly	Lys	Leu>
			C 4 D			c	50			560			570		
530	•		540			٥.	•	•	-	*		•	•		•
TTT	CAA	TCA	GTA	GAG	GTC	TTG	TCA	AAA	GCA	GCT	AAA	GAG	ATG	CTT	GCT
AAA	CTT	AGT	CAT	CTC	CAG	AAC	AGT	TTT	CGT	CGA	TTT	CTC	TAC	GAA	CGA
Phe	Glu	Ser	Val	Glu	Val	Leu	Ser	Lys	Ala	Ala	Lys	Glu	Met	Leu	Ala>
										. م	. ^			:20	
58	0	_		590			600			6.	10		,	20	
አአጥ	- ጥርል	CTT		CAG	CTT	ACA	AGC	CCT	GTT	GTG	GCA	GAA	AGT	CCA	AAA
ተተል	AGT	CAA	TTT	CTC	GAA	TGT	TCG	GGA	CAA	CAC	CGT	CTT	TCA	GGT	TIT
Asn	Ser	Val	Lys	Glu	Leu	Thr	Ser	Pro	Val	Val	Ala	Glu	Ser	Pro	Lys>
	630			6	40			650			660			ь	70
•				እእጥ		»cc	AGC		GAC	GAG	AAA	AAC	AGC	GTT	TCA
AAA	CCI	AAC	CAA	. TAT	CAN	TCG	TCG	GAA	CTG	CTC	TTT	TTG	TCG	CAA	AGT
LVS	Pro	LVS	Gln	Asn	Val	Ser	Ser	Leu	Asp	Glu	Lys	Asn	Ser	Val	Ser>
-, -		•	;												
		680			690			7	00			710		_	720
•		*		*	•		*		•	•		•	<b>~</b> 11	* * * * * * * * * * * * * * * * * * * *	330
GTA	GA?	TT	CCI	GGI	GAA	ATG	AAA i	GIT	CIT	CAT	TCC	. AAA	CAA	- ALAN	AAC
CAT	CIV	AA A	. GGA	CCA	CIT	Met	. Tara	. Uni	Len	Val	Ser	Lvs	Glu	Lvs	TTG Asn>
Val	vol	ישע כ	ı PIC	GIY	GIU	1100	. <i></i> , .	, , ,							
		•	730			740			750	)		7	60		
	•		•	•	•	•		•	•		•		•	•	-
AAA	GA	C GG	AA C	S TAC	GAT	CT	AT:	r GC	A AC	A GTA	GAC	AAC	CTI	GAC	CII
TTT	CT	s cc	G TT	TA T	CT/	A GAT	r TAI	A CG	I TG	r CAT	CIC	TIC	. GAA	. C10	GAA
Lys	AS	p G1	у гу	5 1 <b>y</b> )						. va.	r voj	, bys	, Det	. 520	Leu>
					FI	GURE	31	(2 o	f 4)						

PCT/US94/12352

65/133

# B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

770			-	780			79	ο.			80	0			810		
_		•				•		•	•			•		•	•		•
AAA	GGA	AC	CT :	TCT	GAT	AAA	AAC	TAA	GGA	TC	T G	GA (	GTA	CTT	GAA	GGC	GTA
		~	~ .	202	$\sim$	بلملحك	ጥፐር	TTA	CCT	AG	A C	CI (	CAL		CII	ccc	CVI
Lys	Gly	T	nr :	Ser	Asp	Lys	Asn	Asn	Gly	Se	r G	JA,	Val	Leu	GIU	CIÀ	Val>
83	20			8	30			840				85	0		8	360	
	_		•		*		•	•		*			•	•		•	
AAA	GCT	G	AC .	AAA	AGT	AAA	GTA	AAA	TTA	AC	AA	TT	TCT	GAC	GAT	CTA	GGT
		~	mc	THE PERSONS	TC D	Trive	$C\lambda T$	TTT	AAT	TG	T 1	AA	AGA	CIG	CIW	CAI	CCA
Lys	Ala	Α	sp	Lys	Ser	Lys	Val	Lys	Leu	Th	ır 1	ТЕ	ser	ASP	ASP	Sec	Gly>
	870	1			88	30			890				900			9	10
•				•		•	•		•		•	•	•		•		•
CAA	ACC	: A	CA.	CTT	GAA	GTT	TTC	AAA	GAZ	G?	T C	GC	AAA	ACA	CTA	GTA	TCA
	m^		~~	CAA	CTT	CVV	AAG	TTT	CT	י כי	ra (	عابات	111	101	GAI	CA.	WQ I
Gln	Thi	7	hr	Leu	Glu	Val	Phe	Lys	Glu	ı As	sp (	Sly	Lys	Thr	Leu	VEI	Ser>
		92	0.0			930			9	40			9	950			960
•		-			•	•		•		•		•		•		•	•
777	AA	A C	AT	ACT	TCC	AAA	GAC	AAG	TC	A TO	CA A	ACA	GAA	GAA	AAA	TTC	TAA
		m -	· > ~	ጥ⁄ እ	NCC	th that	്രസ്	TTC	. AG	r ac	GT :	161	CII	CII	111	AAC	114
Lys	Ly	s \	/al	Thr	Ser	Lys	Asp	Lys	Se:	r S	er'	Thr	Glu	Glu	Lys	Phe	Asn>
	•		9.	70			980			9	90			10	00		
	•			•	•		•		•		•		•		•		
GAZ	AA A	A (	GGT	GAA	GŢA	TCI	GAP	LAA	TA A	A A	TA	ACA	AGA	GCA	GAC	GG	ACC
CTT	TT 7	T (	CCA	CTI	CAI	, YC	CII	TT	TA	T T	AT	TGT	101	V) =	. CIC	, CC.	TGG
Gli	ı Ly	S	Gly	Glu	. Val	. Sei	Gli	Ly:	5 11	6 I	TE	1111	Arg	AIC	. vəf	, 013	Thr>
1010				1020	)		10	30			10	40			1050	)	
_				1		•		•	•	•		•		•			
AG	A CI	T	GAA	TAC	: AC	A GG	A AT	AA 1	A AG	CG	TA	GGA	TCI	, GG1	A AA	A GC	AAA 1
mc'	T C	<b>A</b>	$\sim$ TT	ነ አጥና	TG	ר ככי	r ta	A TT	T TC	:G (	A'I'.	CCI	AGF	LCC.			3 111
Ar	g Le	ยน	Glu	Ty	r Thi	r Gl	y Il	e Ly	s S€	er F	ısp	Gly	' Sei	GI	y Ly:	2 WT	e Lys>
1	060				1070			108	0			10	90			1100	
_			•	•	◆,		*		•		•		•		•	:	
GA	G G	ΓŢ	TT	AA A	A GG	C TA	T GT	T CI	T G	AA (	GGA	ACT	CI	A AC	T GC	T GA	ጸጸጸ ጸ ፕሞፕ ፕ
~~	-	• •	1 3 5		T	רג כ	מיז מי	A GZ	VA C	rr (	CCT	TG	A GA	1 16	A CG	w CI	
GJ	u V	al	Lev	ı Ly	s Gl	у Ту	r Va	.1 Le	eu G	ıu '	CIA	Th	L	u 111	1 77	a 01	u Lys>
	13	10			1	120			113	0			114	0		1	150
•				•	_	•		•		•		•		•	•	,	•
ΑC	A A	CA	TT	G GI	G GI	T AJ	A G	LA GO	GA A	CT	GTT	, VC	T TT	A AC	C A	A A	TTA T
~/	~~ ~	~~	2.2	C C	ר כא	A T	רד כי	M C	CT T	GΑ	CAA	TG	а аа	TI	.6 11	T. 1	W IW
Tl	nr T	hr'	Le	u Vā	ıl Va	l Ly	s G	lu G	ly T	hr	Val	Th	r Le	u Se	er Ly	/S A	n Ile>

FIGURE 31 (3 of 4)

B-31 OSP C/ B-31 OSP A / B-31 OSP B FUSION

1160 1170 1180 1190 1200 TCA AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT AGT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA Ser Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser> 1220 1230 GCT GCT ACT AAA AAA ACT GCA GCT TGG AAT GAC AGT ACT AGC ACT TTA CGA CGA TGA TTT TTT TGA CGT CGA ACC TTA CTG TCA TGA TCG TGA AAT Ala Ala Thr Lys Lys Thr Ala Ala Trp Asn Asp Ser Thr Ser Thr Leu> 1250 1260 1270 ACA ATT AGT GCT GAC AGC AAA AAA ACT AAA GAT TTG GTG TTC TTA ACA TGT TAA TCA CGA CTG TCG TTT TTT TGA TTT CTA AAC CAC AAG AAT TGT Thr Ile Ser Ala Asp Ser Lys Lys Thr Lys Asp Leu Val Phe Leu Thr> 1300 1310 1320 1330 GAT GGT ACA ATT ACA GTA CAA CAA TAC AAC ACA GCT GGA ACC AGC CTA CTA CCA TGT TAA TGT CAT GTT GTT ATG TTG TGT CGA CCT TGG TCG GAT Asp Gly Thr Ile Thr Val Gln Gln Tyr Asn Thr Ala Gly Thr Ser Leu> 1360 1370 1380 GAA GGA TCA GCA AGT GAA ATT AAA AAT CTT TCA GAG CTT AAA AAC GCT CTT CCT AGT CGT TCA CTT TAA TTT TTA GAA AGT CTC GAA TTT TTG CGA Glu Gly Ser Ala Ser Glu Ile Lys Asn Leu Ser Glu Leu Lys Asn Ala>

1400

TTA AAA TAA AAT TTT ATT Leu Lys \*\*\*>

#### **FUSION SEQUENCE**

B-31 OSP A/ B-31 P-93 (1168-2100)
Sequence Range: 1 to 1720

10 . 20 30 • AAG CAA AAT GTT AGC AGC CTT GAC GAG AAA AAC AGC GTT TCA GTA GAT TTC GTT TTA CAA TCG TCG GAA CTG CTC TTT TTG TCG CAA AGT CAT CTA K Q N V S S L D E K N S V S V D> 50 60 70 . 80\_\_\_. TTG CCT GGT GAA ATG AAA GTT CTT GTA AGC AAA GAA AAA AAC AAA GAC AAC GGA CCA CTT TAC TTT CAA GAA CAT TCG TTT CTT TTT TTG TTT CTG L P G E M K V L V S K E K N K D> 120 130 110 GGC AAG TAC GAT CTA ATT GCA ACA GTA GAC AAG CTT GAG CTT AAA GGA CCG TTC ATG CTA GAT TAA CGT TGT CAT CTG TTC GAA CTC GAA TTT CCT G K Y D L I A T V D K L E L K G> 170 160 150 180 ACT TCT GAT AAA AAC AAT GGA TCT GGA GTA CTT GAA GGC GTA AAA GCT TGA AGA CTA TTT TTG TTA CCT AGA CCT CAT GAA CTT CCG CAT TTT CGA T S D K N N G S G V L E G V K A> 210 200 230 220 GAC AAA AGT AAA GTA AAA TTA ACA ATT TCT GAC GAT CTA GGT CAA ACC CTG TTT TCA TTT CAT TTT AAT TGT TAA AGA CTG CTA GAT CCA GTT TGG D K S K V K L T I S D D L G Q T> 260 270 250 280 ACA CTT GAA GTT TTC AAA GAA GAT GGC AAA ACA CTA GTA TCA AAA AAA TGT GAA CTT CAA AAG TTT CTT CTA CCG TTT TGT GAT CAT AGT TTT TTT T L E V F K E D G K T L V S K K> 300 310 320 330 GTA ACT TCC AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAT GAA AAA CAT TGA AGG TTT CTG TTC AGT AGT TGT CTT TTT AAG TTA CTT TTT V T S K D K S S T E E K F N E K> 370 350 360 • GGT GAA GTA TCT GAA AAA ATA ATA ACA AGA GCA GAC GGA ACC AGA CTT CCA CTT CAT AGA CTT TTT TAT TAT TGT TCT CGT CTG CCT TGG TCT GAA G E V S E K I I T R A D G T R L>

FIGURE 32 (1 of 5)

PCT/US94/12352

WO 95/12676

68/133

B-31 OSP A/ B-31 P93

400 410 390 420 GAA TAC ACA GGA ATT AAA AGC GAT GGA TCT GGA AAA GCT AAA GAG GTT CTT ATG TGT CCT TAA TTT TCG CTA CCT AGA CCT TTT CGA TTT CTC CAA E Y T G I K S D G S G K A K E V> 450 460 470 440 480 TTA AAA GGC TAT GTT CTT GAA GGA ACT CTA ACT GCT GAA AAA ACA ACA AAT TTT CCG ATA CAA GAA CTT CCT TGA GAT TGA CGA CTT TTT TGT TGT L K G Y V L E G T L, T-A, E K T T> 490 500 510 520 TTG GTG GTT AAA GAA GGA ACT GTT ACT TTA AGC AAA AAT ATT TCA AAA AAC CAC CAA TIT CIT CCT TGA CAA TGA AAT TCG TIT TTA TAA AGT TIT LVVKEGTVTLSKNISK> 550 530 540 560 570 TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT GCT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA CGA S G · E V S V E L N D T D S S A A> 610 590 600 ACT AAA AAA ACT GCA GCT TGG AAT TCA GGC ACT TCA ACT TTA ACA ATT TGA TTT TTT TGA CGT CGA ACC TTA AGT CCG TGA AGT TGA AAT TGT TAA T K K T A A W N S G T S T L T I> 640 650 630 660 ACT GTA AAC AGT AAA AAA ACT AAA GAC CTT GTG TTT ACA AAA GAA AAC TGA CAT TTG TCA TTT TTT TGA TTT CTG GAA CAC AAA TGT TTT CTT TTG T V N S K K T K D L V F T K E N> 680 690 700 ACA ATT ACA GTA CAA CAA TAC GAC TCA AAT GGC ACC AAA TTA GAG GGG TGT TAA TGT CAT GTT ATG CTG AGT TTA CCG TGG TTT AAT CTC CCC T I T V Q Q Y D S N G T K L E G> 740 750 TCA GCA GTT GAA ATT ACA AAA CTT GAT GAA ATT AAA AAC GCT TTA AAA AGT CGT CAA CTT TAA TGT TTT GAA CTA CTT TAA TTT TTG CGA AAT TTT S A V E I T K L D E I K N A L K>

FIGURE 32 (2 of 5)

B-31 OSP A/ B-31 P-93

770			780			79	0		8	300			810		
•		•	•		•		•	•		•		•	•		•
GGT	CAC	CCC	ATG	GAT	GAA	AAG	CTT	TTA	AAA	AGT	AAA	GAT	GAT	ጸጸጸ	GCA
CCA	GTG	GGG	TAC	CTA	CTT	TTC				TCA					CGT
G	H	P	M	D	E	K	L	L	K	s	K	D	D	K	A>
82	20	_	ε	30			840		•	85	0	•	ε	60	
3.00		CAT	CCT	222	ccc	TTC:	CAT	CTT	CAT	CGA	CAA	TTA	TEE	TCT	444
TC)	<b>777</b>	CTA	CCA	ጥጥ	CCC	244	CTA	GAA	CTA	GCT	CTT	TAA	TTA	AGA	TTT
· S	K									R				S	K> .
	••	_	_		•••	_	_		<b>:</b>		•				
	870			88	30		8	90		,	900		_	9:	10
•	•		•		•	•		*		•	•		•		•
										GAA					
			TTT							CTT			I		K>
A	S	S	v	£	Λ.	3	N.	^	ħ		L	_	-	•	11.7
		920			930			9.	40		9	950			960
•		•		• ,	•		•		•	•		•		•	•
GGT	AAG	TCA	CAG	AAA	AGC	TTA	GGC	GAT	TTG	AAT.	AAT	GAT	GAA	AAT	CTT
										TTA					
G	K	S	Q	K	S	L	G	D	L	N	N	D	E	N	L>
		9	70		9	980			990			100	00		
	•	_	•	•		•		•	•		•		•	•	
ATG	ATG	CCA	GAA	GAT	CAA	AAA	TTA	CCT	GAG	GTT	AAA	AAA	TTA	GAT	AGC <sub>.</sub>
TAC	TAC	GGT	CTT							CAA					
M	M	P	E	D	Q	K	L	P	E	V	K	K	L	D	S>
1010			1020			10	30		1	040		:	1050		
•		•	•		•		•	•		•		•	•		•
															ATT
TTT	TTT	CTT	, YYY	TTT						CTC					
K	K	E	F	K	P	V	S	Ε	V	£	K	L	D	K	1>
10	60		1	070			1080			10	90		1	100	
	•	•	•	•		•	*		•		•	•		•	•
TTC	AAG	TCI	TAA :	, yyc	AAT	GTT	GGA	GAZ	TT!	TCA	CCG	TTA	GAT	AAA	TCT
															AGA
F	K	S	N	N	N	V	G	E	L	s	P	L	D	K	S>
	1110	)		11	.20		1	130			1140	ı		11	.50
•	•	•	•		•	•		•		•	•		•		•
															GTT
AGA	ATA	TT?	CTC	TAP											CAA
S	Y	K	D	I	D	S	K	E	E	T	v	N	K	D	V>

B-31 OSP / B-31 P-93

1160 1170 1180 1190 1200 AAT TTG CAA AAG ACT AAG CCT CAG GTT AAA GAC CAA GTT ACT TCT TTG TTA AAC GTT TTC TGA TTC GGA GTC CAA TTT CTG GTT CAA TGA AGA AAC N L Q K T K P Q V K D Q V T S L> 1230 1210 1220 AAT GAA GAT TTG ACT ACT ATG TCT ATA GAT TCC AGT AGT CCT GTA TTT TTA CTT CTA AAC TGA TGA TAC AGA TAT CTA AGG TCA TCA GGA CAT AAA NEDLTTMSIDSSSPVF> 1270 · 1280 1290 1260 1250 TTA GAG GTT ATT GAT CCA ATT ACA AAT TTA GGA ACT CTT CAA CTT ATT AAT CTC CAA TAA CTA GGT TAA TGT TTA AAT CCT TGA GAA GTT GAA TAA LEVIDPITNLGTLQLI> 1310 1320 1330 GAT TTA AAT ACT GGT GTT AGG CTT AAA GAA AGC ACT CAG CAA GGC ATT CTA AAT TTA TGA CCA CAA TCC GAA TTT CTT TCG TGA GTC GTT CCG TAA D L N T G V R L K E S T Q Q G I> 1370 1380 1350 1360 CAG CGG TAT GGA ATT TAT GAA CGT GAA AAA GAT TTG GTT GTT ATT AAA GTC GCC ATA CCT TAA ATA CTT GCA CTT TTT CTA AAC CAA CAA TAA TTT. Q R Y G I Y E R E K D L V V I K> 1400 1410 1420 1430 1440 ATG GAT TCA GGA AAA GCT AAG CTT CAG ATA CTT GAT AAA CTT GAA AAT TAC CTA AGT CCT TTT CGA TTC GAA GTC TAT GAA CTA TTT GAA CTT TTA M D S G K A K L Q I L D K L E N> 1460 1470 1480 TTA AAA GTG GTA TCA GAG TCT AAT TTT GAG. ATT AAT AAA AAT TCA TCT AAT TIT CAC CAT AGT CTC AGA TTA AAA CTC TAA TTA TIT TTA AGT AGA L K V V S E S N F E I N K N S S> 1510 1520 1530 1490 1500 CTT TAT GTT GAT TCT AAA ATG ATT TTA GTA GCT GTT AGG GAT AAA GAT GAA ATA CAA CTA AGA TTT TAC TAA AAT CAT CGA CAA TCC CTA TTT CTA L Y V D S K M I L V A V R D K D>

B-31 OSP A/ B-31 P-93

1550 1560 1570 1540 1580 AGT AGT AAT GAT TGG AGA TTG GCC AAA TTT TCT CCT AAA AAT TTA GAT TCA TCA TTA CTA ACC TCT AAC CGG TTT AAA AGA GGA TTT TTA AAT CTA S S N D W R L A K F S P K N L D> 1600 1610 1620 GAG TTT ATT CTT TCA GAG AAT AAA ATT ATG CCT TTT ACT AGC TTT TCT CTC AAA TAA GAA AGT CTC TTA TTT TAA TAC GGA AAA TGA TCG AAA AGA EFILSENKIMPFTSFS> 1650 1660 1670 1640 GTG AGA AAA AAT TTT ATT TAT TTG CAA GAT GAG TTT AAA AGT CTA GTT CAC TCT TTT TTA AAA TAA ATA AAC GTT CTA CTC AAA TTT TCA GAT CAA -V R K N F I Y L Q D E F K S L V> 1690 1700 1710 1720 ATT TTA GAT GTA AAT ACT TTA AAA AAA GTT AAG GGT CAC C TAA AAT CTA CAT TTA TGA AAT TTT TTT CAA TTC CCA GTG G I L D V N T L K K V K G H X>

B-31 OSP B/ B-31 P41 (122-234)

OSPB/Fla122-234

Sequence Range: 1 to 1180

30 20 . GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT . A Q K G A E S I G S Q K E N D L> 70 80 \_\_\_\_ 60 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 120 100 110 140 130 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 170 160 150 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 210 220 230 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA A T I D Q V E L K G T S D K N N> 260 270 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 300 310 320 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA L T V S A D L N T V T L E A F D> 360 350 370 380 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT A S N Q K I S S K V T K K Q G S>

#### B-31 OSP B/ B-31 P41 (122-234)

		390			4	00			410			420			4	30
	•	•		•		•	•		•		•	•		•		•
	ATA	ACA	GAG	GAA	ACT	CTC	AAA	GCT	' AAT	AAA	TTA	GAC	TCA	AAG	AAA	TTA
	IAI	T TGT	·E	E	TGA T	GAG L	TTT	CGA	TTA	TTT	TAA	CTG	AGI	, IIC		TAA '
	_	•	-6	£	•	L	K	A	N	K	L	D	S	K.	K	L>
			440			450			4	60					450	
15			•		•	*		•			•		470		•	480
Ξ.	ACA	AGA	TCA	AAC	GGA	ACT	ACA	CTT	GAA	TAC	TCA	CAA	ATA	ACA	GAT	GCT
	TGT T	TCT R	AGT S	1.10	CCT	TGA	TGT	GAA	CTT	ATG	AGT	GTT	TAT	TGT	CTA	CGA
	•	K	3	N	G	T	T	L	E	Y	s	Q	I	T	D	ሉ>
			4	90		:	500			510			5	20		
		•		•	•		•		•	•		•				
	GAC	AAT	GCT	ACA	AAA	GCA	GTA	GAA	ACT	CTA	AAA	AAT	AGC	ATT	AAG	CII
	CTG D	TTA N	COA	101	111	CGI	CAT	CTT	TGA	GAT	TTT	TTA	TCG	TAA	TTC	GAA
	U	14	^	T	K	A	V	E	T	L	K	N	S	I	K	L>
	530			540			5	50		9	560			570		
	*		•	•		•		•	•		•		•			•
	GAA	GGA	AGT	CTT	GTA	GTC	GGA	AAA	ACA	ACA	GTG	GAA	ATT	AAA	GAA	GGT
	CII	CCT	ICA	GAA	CAT	CAG	CCT	TTT	TGT	TGT	CAC	CII	TAA	TTT	CTT	CCA
	L	G	3	ь	V	<b>v</b> .	G	K	T	T	V	E	I	K	E	G>
	5	80		5	590	,		600			61	.0		,	520	
		*	•		•		•	•		•		•	•		•	
	ACT	GTT	ACT	CTA	AAA	AGA	GAA	ATT	GAA	AAA	GAT	GGA	AAA	GTA	AAA	GTC
	T	CAA V	T	GAT L	TTT	TCT	CIT	TAA	CTT	TTT	CTA D	CCT				
	-	•	•	-		I.		1	£	K	D	G	K	v	K	V>
		630			64	0		•	550			660			67	n
	*	•		•		•	•		•		•	•		•	-	
	J-1-1.	TTG	AAT	GAC	ACT	GCA	GGT	TCT	AAC	AAA	AAA	ACA	GGT	AAA	TGG	GAA
	F	AAC L	N	D	T	A	G	AGA	TTG N	TTT		TGT				
			_		-	••	•	3	14	N.	K	T	G	K	W	E>
		6	80			690			70	0		7	10			720
	CNC	3.00	•	١	•	•		•		•	•		•		•	•
	CTG	AGT	AC1	TCC	ACT	TTA	ACA	ATT	AGT	GCT	GAC	AGC	AAA	AAA	ACT	AAA
	D	TCA S	T	S	T	L	L 101	TAA	TCA S	CGA	CTG D	TCG				
					•	_	•	•	3	^	U	S,	K	K	T	K>
			73	0		7	40			750			76	0		
	CAT	<b>Ф</b>	CTC	•	•		•		•	•		•		•	•	
	CTA	TTG	CAC	ANG	ATT TA	ACA TOT	GAT	GGT	ACA	ATT	ACA	GTA	CAA	CAA	TAC	AAC
	D	AAC L	V	F	L	T	D	CCA G	TGT	TAA I	TGT T					
				-	_	-	_	-		_	1	v	U	υ	Y	N>

## B-31 OSP B/ B-31 P41 (122-234)

7	770			780			7	90		1	800			810		
	•		•	•		•		•	•		•		•	•		•
	ACA	GCT	GGA	ACC	AGC	CTA	GAA	GGA	TCA	GCA	AGT	GAA	ATT	AAA	AAT	CTT
	T	CGA A	G	TGĠ	S	GAT				A			IAA	K	TTA N	GAA L>
	•	^	•	•	-	_	L	G	3	<b>^</b> .	3		•	N.	14	r>
	82	20		8	830			840			85	50		1	860	
		•	•		•		•	•		. •		•	•		•	
	ACT	CTC	CIT	AAA	AAC	GCT CGA	TTA	AAA	GGT	CAC	CCC	ATG	GCT	CAA	TAT	AAC
	S	E	L	K	N					H.:				GIT O		TTG N>
	_	_	_	••		••	_	••	•	••	•	••	^	Ų	1	14>
		870			88	30		1	390			900			91	10
	•	•		•		•			•		•	•		•		•
	CAA	ATG	CAC	ATG	ATT	TCA	AAC	AAA	TCT	GCT	TCT	CAA	TAA	GTA	AGA	ACA
	Q	M	H	M	L	AGT S	N	K	AGA S	CGA A	AGA S	0	TTA N	CAT	TCT R	
	•			••	_	Ū	••	••		•	-	V	14	٧	K.	T>
		9	20			930			94	0		9	950			960
	•		•		•	•		•		•	•		•		•	•
	CCA	GAA	GAG	CTT	GGA	ATG TAC	CAG	CCT	GCA	AAA	ATT	AAC	ACA	CCA	GCA	TCA
	A	E	E	L		M	Q		A		TAA	n N	TGT	GGT P	CGT A	
		_					-	-		•••	-	••	•	- 4		3,
			97	70		9	980			990			100	00		
•	~~~	* TC1	-	•	•	•	•	<b>5</b> 000	•	•		•		•	•	
	CTT	TCA	GGG	CTT	CAA GTT	GCG	TCT	TGG	• ACT	TTA	AGA	GTT	CAT	GTT	GGA	GCA
-	CTT GAA L	TCA AGT S	GGG	CTT GAA	CAA GTT O	GCG CGC	TCT AGA	ACC	TGA	TTA	TCT	CAA	CAT GTA	GTT CAA	CCT	CGT
	GAA	AGT	GGG	CTT GAA	GTT	GCG CGC	TCT AGA	ACC	TGA	TTA	TCT	GTT CAA V	CAT GTA	GTT	GGA CCT G	GCA CGT A>
	GAA	AGT	GGG CCC G	CTT GAA	GTT	GCG CGC	TCT AGA	W W	TGA	TTA AAT L	TCT	CAA	CAT GTA H	GTT CAA	CCT	CGT
	GAA L	AGT S	GGG CCC G	CTT GAA L	GTT Q	GCG CGC A	TCT AGA S	ACC W	TGA T	TTA AAT L	TCT R	CAA V	CAT GTA H	GTT CAA V	CCT G	CGT A>
	GAA L 10 ACC	AGT S CAA	GGG CCC G	CTT GAA L 1020	GTT Q GCT	GCG CGC A	TCT AGA S	ACC W 30 • GTA	TGA T	TTA AAT L 10	TCT R 040 TAT	CAA V GCA	CAT GTA H	GTT CAA V 1050	CCT G	CGT A>
	GAA L 10 ACC	AGT S CAA	GGG CCC G	CTT GAA L 1020	GTT Q GCT	GCG CGC A	TCT AGA S 103 GCT CGA	ACC W 30 • GTA	TGA T	TTA AAT L 10 ATT TAA	TCT R 040 TAT	CAA V GCA	CAT GTA H	GTT CAA V 1050	CCT G	CGT A> • GCA CGT
	GAA L 10 ACC TGG T	AGT S CAA GTT Q	GGG CCC G G GAT CTA	CTT GAA L 1020 GAA CTT E	GTT Q GCT CGA A	GCG CGC A	TCT AGA S 103 GCT CGA A	ACC W 30 GTA CAT V	TGA T AAT TTA	TTA AAT L 10 ATT TAA	TCT R 40 TAT ATA	CAA V GCA CGT	CAT GTA H • GCT CGA	GTT CAA V L050 AAT TTA	GTT CAA	CGT A>
	L 10 ACC TGG	AGT S CAA GTT Q	GGG CCC G G GAT CTA	CTT GAA L 1020 GAA CTT E	GTT Q GCT CGA	GCG CGC A	TCT AGA S 103 GCT CGA A	ACC W 30 GTA CAT	TGA T AAT TTA	TTA AAT L 10 ATT TAA	TCT R 40 TAT ATA	CAA V GCA CGT A	CAT GTA H • GCT CGA	GTT CAA V 1050 AAT TTA N	GTT CAA	CGT A> • GCA CGT
	L 10 ACC TGG T	AGT S CAA GTT Q	GGG CCC G GAT CTA D	CTT GAA L 1020 GAA CTT E	GTT Q GCT CGA A	GCG CGC A ATT TAA I	TCT AGA S 103 GCT CGA A	ACC W 30 GTA CAT V	TGA T AAT TTA N	TTA AAT L 10 ATT TAA I	TCT R 040 TAT ATA Y	CAA V GCA CGT A	CAT GTA H GCT CGA A	GTT CAA V LOSO AAT TTA N	GTT -CAA V	CGT A> • GCA CGT A>
	GAA L 10 ACC TGG T 106	AGT S CAA GTT Q CTT	GGG CCC G GAT CTA D	CTT GAA L 1020 GAA CTT E 10	GTT Q GCT CGA A	GCG CGC A ATT TAA I	TCT AGA S 103 GCT CGA A GGA	ACC W 30 GTA CAT V LOB0	TGA T AAT TTA N	TTA AAT L 10 ATT TAA I ACT	TCT R 040 TAT ATA Y 109	CAA V GCA CGT A	CAT GTA H GCT CGA A	GTT CAA V L050 AAT TTA N	GTT CAA V	CGT A> GCA CGT A>
	GAA L 10 ACC TGG T 106	AGT S CAA GTT Q CTT	GGG CCC G GAT CTA D	CTT GAA L 1020 GAA CTT E 10	GTT Q GCT CGA A O70 GGT CCA	GCG CGC A ATT TAA I	TCT AGA S 103 GCT CGA A GGA CCT	GTA CAT V	TGA T AAT TTA N CAA GTT	TTA AAT L 10 ATT TAA I ACT TGA	TCT R 040 TAT ATA Y 109 GCT CGA	CAA V GCA CGT A CAG GTC	CAT GTA H GCT CGA A GCT CGA	GTT CAA V LOSO AAT TTA N 13	GTT -CAA V 100 -CCG GGC	CGT A> GCA CGT A>
	ACC TGG T 106 AAT TTA N	CAA GTT Q CTT GAA L	GGG CCC G GAT CTA D	CTT GAA L 1020 GAA CTT E 10 TCT AGA	GTT Q GCT CGA A O70 GGT CCA G	GCG CGC A ATT TAA I GAG CTC E	TCT AGA S 103 GCT CGA A GGA CCT	GTA CAT V LOBO GCT CGA A	TGA T AAT TTA N CAA GTT Q	TTA AAT L 10 ATT TAA I ACT TGA	TCT R 040 TAT ATA Y 109 GCT CGA A	CAA V GCA CGT A CAG GTC	CAT GTA H GCT CGA A GCT CGA	GTT CAA V LOSO AAT TTA N 13	GTT CAA V	GCA CGT A> GTT CAA V>
	ACC TGG T 106 AAT TTA N	CAA GTT Q CTT GAA	GGG CCC G GAT CTA D	CTT GAA L 1020 GAA CTT E 10 TCT AGA	GTT Q GCT CGA A O70 GGT CCA	GCG CGC A ATT TAA I GAG CTC E	TCT AGA S 103 GCT CGA A GGA CCT	GTA CAT V	TGA T AAT TTA N CAA GTT Q	TTA AAT L 10 ATT TAA I ACT TGA	TCT R 040 TAT ATA Y 109 GCT CGA A	CAA V GCA CGT A CAG GTC	CAT GTA H GCT CGA A GCT CGA	GTT CAA V LOSO AAT TTA N 13	GTT -CAA V 100 -CCG GGC	GCA CGT A> GTT CAA V>
	ACC TGG T 106 AAT TTA N	CAA GTT Q CTT GAA L	GGG CCC G GAT CTA D TTC AAG F	CTT GAA L 1020 GAA CTT E 10 TCT AGA S	GCT CGA A D70 GGT CCA G	GCG CGC A ATT TAA I GAG CTC E	TCT AGA S 103 GCT CGA A GGGA CCT G	GTA CAT V LOBO GCT CGA A	TGA T AAT TTA N CAA GTT Q	TTA AAT L 10 ATT TAA I ACT TGA T	TAT ATA Y 109 GCT CGA A	GCA CGT A CAG GTC Q	CAT GTA H GCT CGA A GCT CGA A	GTT CAA V 1050 AAT TTA N 13 GCA CGT A	GTT -CAA V 100 -CCG GGC P	GCA GCA CGT A> GTT CAA V>
	GAA L 10 ACC TGG T 106 AAT TTA N	CAA GTT Q CTT GAA L	GGG CCC G GAT CTA D TTC AAG F	CTT GAA L 1020 GAA CTT E 10 TCT AGA S	GCT CGA A O70 GGT CCA G	GCG CGC A ATT TAA I GAG CTC E	TCT AGA S 103 GCT CGA A CCT G	GTA CAT V LOBO GCT CGA A 1:	TGA T AAT TTA N CAA GTT Q L30 GCT	TTA AAT L 10 ATT TAA I ACT TGA T	TAT ATA Y 105 GCT CGA A CAG	GCA CGT A CAG GTC Q	CAT GTA H GCT CGA A GCT CGA A	GTT CAA V 1050 AAT TTA N 13 GCA CGT A	GTT CAA V 100 CCG GGC P 115	GCA GCA CGT A> GTT CAA V> ACA

B-31 OSP B/ B-31 P41 (122-234)

GCA CCT TCT CAA GGC GGA GTT GGT CAC C
CGT GGA AGA GTT CCG CCT CAA CCA GTG G
A P S Q G G V G H X>

FIGURE 33 (4 of 4)

76/133 B-31 OSP B / B-31 P41 (122-295)

Sequence Range: 1 to 1363

20 30 10 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT A Q K G A E S I G S Q K E N D L> 60 70 80 60 90 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA-AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 100 110 120 130 • CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 170 150 160 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 200 210 220 230 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA ATIDQVELKGTSDKN N> 260 270 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 310 320 300 290 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA L T V S A D L N T V T L E A F D> 360 370 350 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT A S N Q K I S S K V T K K Q G S>

## B-31 OSP B / B-31 P41 (122-295)

		390	)		4	00			410			420	)			130
	•	•		•		•	•	,	•		•		•	•		_
	ATA	ACA	GAG	GAA	ACT	CIC	AAA :	GCT	TAA '	, YYY	TŢĮ	GAC	TC	AAC	AAA :	TTA
	IMI	101	CIC	. CII	TGA	GAG	177	, CGA	L TTA	TTT	, yyı	CTC	AG	TTC	TIT	ATT A
	I	T	E	E	T	L	K	A	N	K	L	D	s	ĸ		
			440			450			4	60			470			400
, ,,	•		•		•	•		•		•	•				•	480
•	ACA	AGA	TCA	AAC	GGA	ACT	ACA	CTI	GAA	TAC	TCA	CAA	ATA	ACA	GAT	GCT
	101	101	VOI	110	CCI	IGA	161	GAA	CIT	ATG	AGT	'-GTT	TAT	TGT	CTA	GCT CGA
	<b>T</b> .	R	S	N	G	· T	T	L	E	Y	S	Q	I	T	D	
			4	90			500			510			5	20		
		*		•	•		•		•	•		•	_	_ •	•	
	GAC	AAT	GCT	ACA	AAA	GCA	GTA	GAA	ACT	CTA	AAA	AAT	AGC	ATT	AAG	للبلك.
	CIG	IIA	CGA	101	1.1.1.	CGT	CAT	CTT	TGA	GAT	TTT	TTA	TCG	TAA	TTC	GAA
	D	N	A	T	K	A	V	Ε	T	L	K	N	S	I	K	L>
	530			540			5	50			560			570	•	
	•		•	•		•		•	•		•		•			
	GAA	GGA	AGT	CTT	GTA	GTC	GGA	AAA	ACA	ACA	GTG	GAA	ATT	AAA	C A A	GGT
	CII	CCI	ICA	GAA	CAT	CAG	CCT	TTT	TGT	TGT	CAC	CTT	TAA	TTT	CTT	CCA
	E	G	S	L	V	V	G	K	T	T	v	E	I	K	E	G>
	51		590			600			6	10		620				
		•	•		•		*	•		•		•	•		•	
	ACT	GTT	ACT	CTA	AAA	AGA	GAA	ATT	GAA	AAA	GAT	GGA	AAA	GTA	AAA	GTC
	104	CAA	IGA	GAI	111	TCT	CTT	TAA	CTT	TTT	CTA	CCT	TTT	CAT	TTT	CAG
	T	V	T	L	ĸ	R	E	I	E	K	D	G	K	v	ĸ	V>
		630			64	0		(	550			660			67	'n
	•	•		•		•	•		•		•	•		•	-	_
	TTT	TTG	AAT	GAC	ACT	GCA	GGT	TCT	AAC	AAA	AAA	ACA	GGT	AAA	TGG	GAA
	~~~	MAC	IIA	CIG	TGA	CGT	CCA	AGA	TTG	TTT	TTT	TGT	CCA	TTT	ACC	CTT
	r	L	N	D	T	A	G	S	N	K	K	T	G	K	W	E>
٠		6	80			690	•		70	0		7	10			720
	•		*		•	•		•		•	•		•		•	_
	GAC	AGT	ACT	AGC	ACT	TTA	ACA	ATT	AGT	GCT	GAC	AGC	AAA	AAA	ACT	AAA
	CIG	ICA	IGA	TCG	TGA	AAT.	TGT	TAA	TCA	CGA	CTG	TCG	TTT	TTT	TGA	TTT
	Đ	S	T	S	T	L	T	I	S	A	D	S	ĸ	K	T	K>
			73	0		7	40			750	ı		76	:n		
		•		•	•		•		•	•		•		•	•	
	GAT	TTG	GTG	TTC	TTA	ACA	GAT	GGT	ACA	ATT	ACA	GTA	CAA	CAA	TAC	AAC
	CIN	AAC	CAC	AAG	AAT.	TGT	CTA	CCA	TGT	TAA	TGT	CAT	GTT	GTT	ATG	TTG
	D	L	v	F	T.	Т	ת	C	~	T	_					

FIGURE 34 (2 of 4)

The same of

B-31 OSP B / B-31 P41 (122-295)

770		780			790					800			810		
•		•	•		•		•	•		•		•	•		•
AC.	A GCT	GGA	ACC	AGC	CTA	GAA	GGA	TCA	GCA	AGT	GAA	ATT	ጸዱ	AAT	CTT
TG	r CGA	CCT	TGG	TCG	GAT	CTT	CCT	AGT	CGT	TCA	CTT	TAA	TIT	TTA	GAA
T	Α	G	T	S	L	Ε	G	S	A	S	E	I	K	N	Ľ>

820 830 840 850 860

TCA GAG CTT AAA AAC GCT TTA AAA GGT CAC CCC ATG GCT CAA TAT AAC AGT CTC GAA TTT TTG CGA AAT TTT CCA GTG GGG TAC CGA GTT ATA TTG S E L K N A L K G H P M A Q Y N>

870 880 890 900 910

CAA ATG CAC ATG TTA TCA AAC AAA TCT GCT TCT CAA AAT GTA AGA ACA
GTT TAC GTG TAC AAT AGT TTG TTT AGA CGA AGA GTT TTA CAT TCT TGT
Q M H M L S N K S A S Q N V R T>

920 930 940 950 960

GCT GAA GAG CTT GGA ATG CAG CCT GCA AAA ATT AAC ACA CCA GCA TCA
CGA CTT CTC GAA CCT TAC GTC GGA CGT TTT TAA TTG TGT GGT CGT AGT
A E E L G M Q P A K I N T P A S>

970 980 990 1000

CTT TCA GGG CTT CAA GCG TCT TGG ACT TTA AGA GTT CAT GTT GGA GCA
GAA AGT CCC GAA GTT CGC AGA ACC TGA AAT TCT CAA GTA CAA CCT CGT
L S G L Q A S W T L R V H V G A>

1010 1020 1030 1040 1050

ACC CAA GAT GAA GCT ATT GCT GTA AAT ATT TAT GCA GCT AAT GTT GCA TGG GTT CTA CTT CGA TAA CGA CAT TTA TAA ATA CGT CGA TTA CAA CGT T Q D E A I A V N I Y A A N V A>

1060 1070 1080 1090 1100

AAT CTT TTC TCT GGT GAG GGA GCT CAA ACT GCT CAG GCT GCA CCG GTT TTA GAA AAG AGA CCA CTC CCT CGA GTT TGA CGA GTC CGA CGT GGC CAA N L F S G E G A Q T A Q A A P V>

1110 1120 1130 1140 1150

CAA GAG GGT GTT CAA CAG GAA GGA GCT CAA CAG CCA GCA CCT GCT ACA GTT CTC CCA CAA GTT GTC GGT CGT GGA CGA TGT Q E G V Q Q E G A Q Q P A P A T>

FIGURE: 34 (3 of 4)

#### B-31 OSP B / B-31 P41 (122-295)

..... 1170 1180 1190 1200 1160 GCA CCT TCT CAA GGC GGA GTT AAT TCT CCT GTT AAT GTT ACA ACT ACA CGT GGA AGA GTT CCG CCT CAA TTA AGA GGA CAA TTA CAA TGT TGA TGT A P S Q G G V N S P V N V T T T> 1210 1220 1230 • • • GTT GAT GCT AAT ACA TCA CTT GCT AAA ATT GAA AAT GCT ATT AGA ATG CAA CTA CGA TTA TGT AGT GAA CGA TTT TAA CTT TTA CGA TAA TCT TAC V D A N T S L A K I E E N A I R M> 250 1260 1270 1280 1250 1290 • ATA AGT GAT CAA AGG GCA AAT TTA GGT GCT TTC CAA AAT AGA CTT GAA TAT TCA CTA GTT TCC CGT TTA AAT CCA CGA AAG GTT TTA TCT GAA CTT I S D Q R A N L G A F Q N R L E> 1300 1310 1320 1330 TCT ATA AAG AAT AGT ACT GAG TAT GCA ATT GAA AAT CTA AAA GCA TCT AGA TAT TTC TTA TCA TGA CTC ATA CGT TAA CTT TTA GAT TTT CGT AGA S I K N S T E Y A I E N L K A S> 1350 1360 TAT GCT CAA ATA GGT CAC C ATA CGA GTT TAT CCA GTG G Y A Q I G H X>

PCT/US94/12352

WO 95/12676

80/133

B-31 OSP B/ B-31 P41 (140-234)

Sequence Range: 1 to 1141

20 30 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT AQKGAESIGSQKENDL> 60 70 80 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CIT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 120 110 100 130 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 170 160 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L. R> 200 210 220 230 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA A T I D Q V E L K G T S D K N N> 250 260 270 280 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AA2 CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 300 310 320 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA LTVSADLNTVTLEAFD 350 360 350 360 370 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT A S N Q K I S S K V T K K Q G S>

PCT/US94/12352

WO 95/12676

81/133

B-31 OSP B/ B-31 P41 (140-234)

400 410 . 420 390 ATA ACA GAG GAA ACT CTC AAA GCT AAT AAA TTA GAC TCA AAG AAA TTA TAT TGT CTC CTT TGA GAG TTT CGA TTA TTT AAT CTG AGT TTC TTT AAT I T E E T L K A N K L D S K K L> 460 470 450 440 • ACA AGA TCA AAC GGA ACT ACA CTT GAA TAC TCA CAA ATA ACA GAT GCT TGT TCT AGT TTG CCT TGA TGT GAA CTT ATG AGT GTT TAT TGT CTA CGA TRSNGTTLEYS\_QITDA> 500 . 510 520 490 GAC AAT GCT ACA AAA GCA GTA GAA ACT CTA AAA AAT AGC ATT AAG CTT CTG TTA CGA TGT TTT CGT CAT CTT TGA GAT TTT TTA TCG TAA TTC GAA D N A T K A V E T L K N S I K L> 540 550 560 GAA GGA AGT CTT GTA GTC GGA AAA ACA ACA GTG GAA ATT AAA GAA GGT CTT CCT TCA GAA CAT CAG CCT TTT TGT TGT CAC CTT TAA TTT CTT CCA EGSLVVGKTTVEIKEG> 580 590 600 610 620 ACT GTT ACT CTA AAA AGA GAA ATT GAA AAA GAT GGA AAA GTA AAA GTC TGA CAA TGA GAT TTT TCT CTT TAA CTT TTT CTA CCT TTT CAT TTT CAG T V T L K R E I E K D G K V K V> 660 640 650 TTT TTG AAT GAC ACT GCA GGT TCT AAC AAA AAA ACA GGT AAA TGG GAA AAA AAC TTA CTG TGA CGT CCA AGA TTG TTT TTT TGT CCA TTT ACC CTT F L N D T A G S N K K T G K W E> 700 680 690 700 710 GAC AGT ACT AGC ACT TTA ACA ATT AGT GCT GAC AGC AAA AAA ACT AAA CTG TCA TGA TCG TGA AAT TGT TAA TCA CGA CTG TCG TTT TTT TGA TTT D S T S T L T I S A D S K K T K> 730 740 750 GAT TTG GTG TTC TTA ACA GAT GGT ACA ATT ACA GTA CAA CAA TAC AAC CTA AAC CAC AAG AAT TGT CTA CCA TGT TAA TGT CAT GTT ATG TTG D L V F L T D G T I T V Q Q Y N>

FIGURE 35 (2 of 3)

### B-31 OSP B/ B-31 P41 (140-234)

									,				010		•
770		_	780			79	•	•	Ł	300		•	810		
	ccm	CCN	200	AGC	CTA	CAA	CCA	<b>ፐር</b> ኔ	CCA	ACT.	CAA	ልጥ	222	דבג	
				TCG											
T	A	G	T	s	L	E	G	s	A	s	E	I	К	N	L>
•	^	•	•	•	_	_	•	•		_	_	_			
82	20		8	330			840			85	50		8	360	
	•	•		•		•	•		*		•	•		•	
				AAC											
AGT	CTC	GAA	TTT	TTG	CGA	AAT	TTT	CCA	GTG	GGG	TAC	CGA	AGA	GTT	TTA
S	E	L	K	N	A	L	K	G	Н	P	M	A	S	Q	N>
							,				000				
_	870			88	*		•	90			900		•	9.	10
CW.	303	202	- CCW	GAA	CAG	لىلىل	CGA	DT4	CAG	ССТ	GC2	444	ልጥጥ	220	)C)
				CTT											
V		T		E			G	М		P	A	К	I	N	T>
•	••	•	••	_	_	_	•		•	_			_		
	!	920			930			94	40		9	950		•	960
•		•		•	•		•		•	*		•		•	•
				TCA											
GGT	CGT	AGT	GAA	AGT									TCT	CAA	GTA
P	A	S	L	S	G	L	Q	Α.	S	W	T	L	R	V	H>
		٥.	70			980			990			100	20		
	•	,	•	•	•	•		•	*			101	•	•	
GTT	GGA	GCA	ACC	САА	GAT	ĠAA	GCT	ATT	GCT	GTA	AAT	ATT	TAT	GCA	GCT
				GTT											
v	G	A	T	Q	D		A		Α		N	· 1	Y	Α	λ>
1010			1020		_	10	30	_	1	040		. :	1050		
	c mm	*		CTT	TTC	TOTAL	-	CAC	CCN		CNN	» V	-	CNC	CCT
				GAA											
, N	V	A	N		F	S			G	A	Q	T	A	Q	A>
. ••	•		•••	_	•	_	Ū	_	<b>.</b>	••	•	•	••	¥	•••
10	60		1	070			1080			10	90		1	100	
	•	•		•		•	•		••		•	•		•	
GCA	CCG	GTT	CAA	GAG	GGT	GTT	CAA	CAG	GAA	GGA	ĢCT	CAA	CAG	CCA	GCA
															CGT
A	P	v	Q	E	G	V	Q	Q	E	G	A	Q	Q	P	A>
	1117				20		. 1	130			1140				
	1110		•		20	*	. 1	* 120		•					
				CCT								С			
				GGA											
					S										

FIGURE 35 (3 of 3)

PCT/US94/12352

83/133

B-31 OSP B/ B-31 P41 (140 -295)

Sequence Range: 1 to 1324

10 20 30 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT AQKGAESIGSQKENDL> 60 70 • • • 70 80 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 110 120 130 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 150 160 170 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 200 210 220 230 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA A T I D Q V E L K G T S D K N N> 260 250 270 280 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 290 320 300 310 330 • TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA L T V S A D L N T V T L E A F D> 350 360 370 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT ASNQKISSKVTKKQGS>

FIGURE 36 (1 of 4)

### B-31 OSP B/ B-31 P41 (140 -295)

		390			4	00			410			420			4	30
	• .	•		•		•	*		•		•	•		•		•
	ATA	ACA	GAG	GAA	ACT	CTC	AAA	GCT	AAT	AAA	TTA	GAC	TCA	λAG	AAA	TTA
	TAT	TGT	CTC	CTT	TGA	GAG	TTT	CGA	TTA	TTT	AAT	CTG	AGT	TTC	TTT	AAT
	I	T	E	E	T	L	K	A	N	K	L	D	S	K	K	L>
			440			450			4	60			470			480
4	. •		•		•	•		•		•	•		•		•	•
•	ACA	AGA	TCA	AAC	GGA	ACT	ACA	CTT	GAA	TAC	TCA	CAA	ATA	ACA	GAT	GCT
	TGT	TCT	AGT	TTG	CCT	TGA	TGT	GAA	CTT	ATG	AGT	GTT	TAT	TGT	CTA	CGA
	T	R	S	N	G	T	T	L	E	¥	· s-	Q -	I	T		A>
			45	90		9	500			510			5	20		•
		•		•	•		•		•	•		•		•	•	
	GAC	AAT	GCT	ACA	AAA	GCA	GTA	GAA	ACT	CTA	AAA	AAT	AGC	ATT	AAG	CTT
	CTG	TTA	CGA	TGT	TTT	CGT	CAT	CTT	TGA	GAT	TTT	TTA	TCG	TAA	TTC	GAA
	D	N	Α	T	K	A		E	T	L	K	N	s	I		L>
	530			540			51	50			560			570		
	•		•	•		•		•	•	•	•		•	370		•
	GAA	GGA	AGT	CTT	GTA	GTC	GGA	AAA	ACA	ACA	GTG	GAA	ATT	222	CAA	CCT
	CTT	CCT	TCA	GAA	CAT	CAG	CCT	TTT	TGT	TGT	CAC	CTT	TAA	TTT	CTT	CCV
	E	G	S	L	v	v			T		V		I	ĸ	E	G>
	58	30		:	590			600			6:	10			520	
		•	•		•		•	•		•		•	•		•	
	ACT	GTT	ACT	CTA	AAA	AGA	GAA	ATT	GAA	AAA	GAT	GGA	AAA	GTA	λλλ	GTC
	TGA	CAA	TGA		TTT	TCT	CTT	TAA	CTT	TTT	CTA	CCT	TTT	CAT	TTT	CAG
	T	V	T	L	ĸ	R	E.	I	E	K	D	G.	K	V	K	٧>
		630			64	0		6	50			660			67	20
	•	•		•		•	•		•		•	•		•		•
	TTT	TTG	TAA	GAC	ACT	GCA	GGT	TCT	AAC	AAA	AAA	ACA	GGT	AAA	TGG	GAA
	AAA	AAC	TTA	CTG	TGA	CGT	CCA	AGA	TTG	TTT	TTT	TGT	CCA	TTT	ACC	CTT
	F	L	N	Ð	T	A	G	S	N	K	K	T	G	K	W	E>
		. 6	680			690			70	0		7	7.10			720
	•		•		•	•		•		•	•		•		•	•
	GAC	AGT	ACT	AGC	ACT	TTA	ACA	TTA	AGT	GCT	GAC	AGC	AAA	AAA	ACT	AAA
	CTG	TCA	TGA	TCG	TGA	AAT	TGT	TAA	TCA	CGA	CIG	TCG	TTT	TTT	TGA	TTT
	D	S	T	S	T	L	T	I	S	A	D	S	K	K	T	K>
			73	0		7	40			750			76	50		
	~ · ·	- T	055		*		•		•	•		•		•	•	
	GAT	116	GTG	TIC	TTA	ACA	GAT	GGT	ACA	ATT	ACA	GTA	CAA	CAA	TAC.	AAC
	D	AAC L	V	AAG F	AAT L		CTA D								ATG V	
	u	-	v	r	1.	1.	13	G	11.	ſ	414	17	$\sim$	$\sim$	37	

FIGURE 36 (2 of 4)

### B-31 OSP B/ B-31 P41 (140 -295)

770			780			79	90		8	300			810		
•		•	•		•		•	•		•		•	•		•
		GGA													
TGT	CGA	CCT	TGG							TCA	CTT	AAT	TTT	TTA	GAA
T	A	G	T	s	L	E	G	S	λ	S	E	I	K	N	L>
. 82	20		8	330		_	840			85	50	_	8	360	
	•	~~~			CCT	TTA	***	CCT	C3.C		• •		m~m	~``	
		CTT GAA													
NG1	E	L	K		A					ĝ"			S		N>
3	L	U	K	••	^	_	••	•	••	٠	**	•	3	¥	147
	870			88	30 ·		8	390			900			9:	10
•	•		•		*	•		*		•	•		•		•
		ACA TGT													
V		T			E					P		K	I	N	
v	K	•	^		L	-	•	11	~	•	^	, A	-	14	13
	9	920			930			94	10		9	950			960
•		•		•	•		•		•	•		•		•	•
		TCA													
		AGT													
P	Α	S	L	S	G	L	Q	Α	S	W	Т	L	R	V	Н>
		91	70		9	980			990			100	00		
	•	91	70	•	9	980		•	990		•	100	•	•	
GTT	• GGA	91 GCA	•	• CAA		*	GCT	• ATT	•	GTA	AAT		•	• GCA	GCT
			ACC	GTT	GAT CTA	GAA CTT	CGA	TAA	GCT CGA	CAT	TTA	ATT	TAT		
	CCT	GCA	ACC TGG	GTT	GAT	GAA CTT	CGA	TAA	GCT CGA	CAT	TTA	ATT	TAT		CGA
CAA	CCT	GCA ÇGT A	ACC TGG	GTT Q	GAT CTA	GAA CTT	CGA A	TAA	GCT CGA A	CAT	TTA N	ATT TAA I	TAT ATA	CGT	CGA
CAA V 1010	CCT G	GCA ÇGT A	ACC TGG T	GTT Q	GAT CTA D	GAA CTT E	CGA A 30	TAA I	GCT CGA A	CAT V 040	TTA N	ATT TAA I	TAT ATA Y	CGT A	CGA A>
CAA V 1010 • AAT	CCT G	GCA ÇGT A	ACC TGG T	GTT Q CTT	GAT CTA D	GAA CTT E	CGA A 30 • GGT	TAA I • GAG	GCT CGA A	CAT V 040 GCT	TTA N CAA	ATT TAA I ACT	TAT ATA Y 1050 GCT	CGT A CAG	CGA A> GCT
CAA V 1010 AAT TTA	CCT G GTT CAA	GCA ÇGT A • GCA CGT	ACC TGG T 1020 AAT	GTT Q CTT GAA	GAT CTA D TTC AAG	GAA CTT E 10: TCT AGA	CGA A 30 GGT CCA	TAA I GAG CTC	GCT CGA A 1 GGA CCT	CAT V 040 GCT CGA	TTA N CAA GTT	ATT TAA I ACT TGA	TAT ATA Y 1050 GCT CGA	CAG GTC	CGA A> • GCT CGA
CAA V 1010 • AAT	CCT G	GCA ÇGT A	ACC TGG T	GTT Q CTT	GAT CTA D TTC AAG	GAA CTT E	CGA A 30 GGT CCA	TAA I GAG CTC	GCT CGA A 1 GGA CCT	CAT V 040 GCT	TTA N CAA GTT	ATT TAA I ACT TGA	TAT ATA Y 1050 GCT	CAG GTC	CGA A> GCT
CAA V 1010 AAT TTA	GTT CAA	GCA ÇGT A • GCA CGT	ACC TGG T 1020 AAT TTA N	GTT Q CTT GAA	GAT CTA D TTC AAG	GAA CTT E 10: TCT AGA S	CGA A 30 GGT CCA	TAA I GAG CTC E	GCT CGA A 1 GGA CCT	CAT V 040 GCT CGA	TTA N CAA GTT Q	ATT TAA I ACT TGA	TAT ATA Y 1050 GCT CGA A	CAG GTC	CGA A> • GCT CGA
CAA V 1010 AAT TTA N	GTT CAA V	GCA CGT A GCA CGT A	ACC TGG T 1020 AAT TTA N	CTT GAA L .	GAT CTA D TTC AAG F	GAA CTT E 10: TCT AGA S	CGA A 30 GGT CCA G	TAA I GAG CTC E	GCT CGA A 1 GGA CCT G	CAT V 040 GCT CGA A	TTA N CAA GTT Q	ATT TAA I ACT TGA T	TAT ATA Y 1050 GCT CGA A	CAG GTC Q	CGA A> GCT CGA A>
CAA V 1010 • AAT TTA N 100	GTT CAA V	GCA CGT A GCA CGT A	ACC TGG T 1020 AAT TTA N	GTT Q CTT GAA L	GAT CTA D TTC AAG F	GAA CTT E 10: TCT AGA S	CGA A 30 GGT CCA G 1080 CAA	TAA I GAG CTC E	GCT CGA A 1 GGA CCT G	CAT V 040 GCT CGA A 100	TTA N CAA GTT Q 90 • GCT	ATT TAA I ACT TGA T	TAT ATA Y 1050 GCT CGA A 1:	CAG GTC Q	CGA A> GCT CGA A>
CAA V  1010 AAT TTA N  100 GCA CGT	GTT CAA V CCG GGC	GCA CGT A GCA CGT A	ACC TGG T 1020 AAT TTA N 1 CAA GTT	GTT Q CTT GAA L 070 GAG CTC	GAT CTA D TTC AAG F	GAA CTT E 10: TCT AGA S	CGA A 30 GGT CCA G 1080 CAA GTT	TAA I GAG CTC E CAG GTC	GCT CGA A 1 GGA CCT G	CAT V 040 GCT CGA A 109 GGA CCT	CAA GTT Q GCT CGA	ATT TAA I ACT TGA T CAA GTT	TAT ATA Y 1050 GCT CGA A 12 CAG GTC	CGT A CAG GTC Q 100 CCA GGT	CGA A> GCT CGA A> GCA CGT
CAA V 1010 • AAT TTA N 100	GTT CAA V CCG GGC	GCA CGT A GCA CGT A	ACC TGG T 1020 AAT TTA N	GTT Q CTT GAA L	GAT CTA D TTC AAG F	GAA CTT E 10: TCT AGA S	CGA A 30 GGT CCA G 1080 CAA	TAA I GAG CTC E CAG GTC	GCT CGA A 1 GGA CCT G	CAT V 040 GCT CGA A 109 GGA CCT	CAA GTT Q GCT CGA	ATT TAA I ACT TGA T	TAT ATA Y 1050 GCT CGA A 12 CAG GTC	CGT A CAG GTC Q 100 CCA GGT	CGA A> GCT CGA A> GCA CGT
CAA V 1010 * AAT TTA N 100 GCA CGT A	GTT CAA V CCG GGC	GCA CGT A GCA CGT A GTT CAA V	ACC TGG T 1020 AAT TTA N 1 CAA GTT	GTT Q CTT GAA L 070 GAG CTC	GAT CTA D TTC AAG F GGT CCA G	GAA CTT E 10: TCT AGA S	CGA A 30 GGT CCA G 1080 CAA GTT Q	TAA I GAG CTC E CAG GTC	GCT CGA A 1 GGA CCT G	CAT V 040 GCT CGA A 109 GGA CCT G	CAA GTT Q GCT CGA	ATT TAA I ACT TGA T CAA GTT Q	TAT ATA Y 1050 GCT CGA A 12 CAG GTC	CGT A CAG GTC Q 100 CCA GGT	CGA A> GCT CGA A> GCA CGT A>
CAA V 1010 AAT TTA N 100 GCA CGT A	GTT CAA V 60 . CCG GGC P	GCA CGT A GCA CGT A GTT CAA V	ACC TGG T 1020 AAT TTA N 1 CAA GTT Q	CTT GAA L GAG CTC E 11	GAT CTA D TTC AAG F GGT CCA G	GAA CTT E 100 TCT AGA S GTT CAA V	CGA A 30 GGT CCA G 1080 CAA GTT Q	GAG CTC E CAG GTC Q	GCT CGA A 10 GGA CCT G GAA CTT E	CAT V 040 GCT CGA A 100 GGA CCT G	CAA GTT Q 90 GCT CGA A	ATT TAA I ACT TGA T CAA GTT Q	TAT ATA Y 1050 GCT CGA A 1: CAG GTC Q	CAG GTC Q 100 CCA GGT P	GCA GCA GCA GCA CGT A>
CAA V 1010 * AAT TTA N 100 GCA CGT A	GTT CAA V 60 . CCG GGC P	GCA CGT A GCA CGT A GTT CAA V	ACC TGG T 1020 AAT TTA N 1 CAA GTT Q	CTT GAA L	GAT CTA D TTC AAG F GGT CCA G	GAA CTT E 10: TCT AGA S GTT CAA V	CGA A 30 GGT CCA G 1080 CAA GTT Q 1 GGC	GAG CTC E CAG GTC Q 130 GGA	GCT CGA A 10 GGA CCT G GAA CTT E	CAT V 040 GCT CGA A 100 GGA CCT G	CAA GTT Q 90 GCT CGA A 1140	ATT TAA I ACT TGA T CAA GTT Q	TAT ATA Y 1050 GCT CGA A 11 CAG GTC Q	CAG GTC Q 100 CCA GGT P	CGA A> GCT CGA A> GCA CGT A> GCA CGT A>
CAA V 1010 AAT TTA N 100 GCA CGT A CCT GGA	GTT CAA V 60 . CCG GGC P	GCA CGT A GCA CGT A GTT CAA V	ACC TGG T 1020 AAT TTA N 1 CAA GTT Q	CTT GAA L	GAT CTA D TTC AAG F GGT CCA G	GAA CTT E 10: TCT AGA S GTT CAA V	CGA A 30 GGT CCA G 1080 CAA GTT Q 1 GGC CCG	GAG CTC E CAG GTC Q 130 GGA	GCT CGA A 10 GGA CCT G GAA CTT E	CAT V 040 GCT CGA A 100 GGA CCT G	CAA GTT Q 90 GCT CGA A 1140	ATT TAA I ACT TGA T CAA GTT Q CCT GGA	TAT ATA Y 1050 GCT CGA A 11 CAG GTC Q	CAG GTC Q 100 CCA GGT P	CGA A> GCT CGA A> GCA CGT A> GCA CGT A>

FIGURE 36 (3 of 4)

B-31 OSP B/ B-31 P41 (140 -295)

1170 1180 1190 1160 ACA ACT ACA GTT GAT GCT AAT ACA TCA CTT GCT AAA ATT GAA AAT GCT TGT TGA TGT CAA CTA CGA TTA TGT AGT GAA CGA TTT TAA CTT TTA CGA T T T V D A N T S L A K I E N A> 1230 1220 1210 ATT AGA ATG ATA AGT GAT CAA AGG GCA AAT TTA GGT GCT TTC CAA AAT TAA TCT TAC TAT TCA CTA GTT TCC CGT TTA AAT CCA CGA AAG GTT TTA IRMISDQRANLGAFQN> 1270 1260 1280 AGA CTT GAA TCT ATA AAG AAT AGT ACT GAG TAT GCA ATT GAA AAT CTA TCT GAA CTT AGA TAT TTC TTA TCA TGA CTC ATA CGT TAA CTT TTA GAT R L E S I K N S T E Y A I E N L> 1320 1300 1310 AAA GCA TCT TAT GCT CAA ATA GGT CAC C TTT CGT AGA ATA CGA GTT TAT CCA GTG G K A S Y A Q I G H X>

Osp b/ fla (122-234) osp c Sequence Range: 1 to 1765

> 30 20 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT A Q K G A E S I G S Q K E N D L> 80 80 70 60 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 120 110 100 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 160 170 180 190 150 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 200 210 220 230 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA A T I D Q V E L K G T · S D K N N> 270 260 250 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 320 310 330 300 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA L T V S A D L N T V T L E A F D> 370 350 . 360 • GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT A S N Q K I S S K V T K K Q G S>

> > FIGURE 37 (1 of 5)

Osp b/ fla (122-234) osp c

•	390		•	40	00		•	110		•	420		•	4:	30
		C1C	C	3 C-70	cmc										-
WIW	ACA	CMC	CATA	WC1	CIC	AAA	CCI	MAI	AAA	114	GAC	ICA	AAG	AAA	TTA
									TTT						
Ţ	T	E	£	T	L	K	A	N	K	L	D	S	K	K	L>
	4	140			450			4			4	470			480
•	•				•		•		•	•		•		•	•
ACA	AGA	TCA	AAC	GGA	ACT	ACA	CTT	GAA	TAC	TCA	CAA	ATA	ACA	GAT	GCT
TGT			TTG	CCT	TGA	TGT	GAA	CTT	ATG	AGT	GTT	TAT	TGT	CTA	CGA
T	R	S	N	G	T	T	L		Y			I	T	D	λ>
						•			. =	<u> </u>	•				
		4	90		5	500			510			52	20		
	• .		•	•		•		•	•		•		•	•	
GAC	TAA	GCT	ACA	AAA	GCA	GTA	GAA	ACT	CTA	AAA	AAT	AGC	ATT	AAG	CTT
CTG	TTA	CGA	TGT	TTT	CGT	CAT	CTT	TGA	GAT	TTT	TTA	TCG	TAA	TTC	GAA
D	N	A	T	K	A	V	E	T	L	K	N	S	I	ĸ	L>
530			540			55	50			560			570		
•		•	•		•		•	•		•		•	•		•
GAA	GGA	AGT	CTT	GTA	GTC	GGA	AAA	ACA	ACA	GTG	GAA	ATT	AAA	GAA	GGT
CTT	CCT	TCA	GAA	CAT	CAG	CCT	TTT	TGT	TGT	CAC	CTT	TAA	TIT	CTT	CCA
E	G	S	L	V	v	G	K	T	T	v	E	I	ĸ	Ξ	G>
	•														
58	80			590			600			6:	10		6	520	
	•	•		•		•	•		•		•	•		•	
ACT	GTT	• ACT	СТА	· AAA	AGA	• GAA	TTA	GAA	• AAA	GAT	• GGA	• AAA	GTA	AAA	GTC
ACT TGA	GTT CAA	TGA	CTA GAT	AAA TTT	TCT	• GAA CTT	TTA	CTT	TTT	GAT CTA	• GGA CCT	TTT	GTA	AAA	GTC CAG
ACT TGA	GTT	TGA	CTA GAT	AAA TTT	TCT	• GAA CTT	TTA	CTT	AAA TTT ,K	GAT CTA	• GGA CCT	TTT	GTA CAT	AAA	CAG
ACT TGA	GTT CAA V	TGA	CTA GAT	AAA TTT K	TCT R	• GAA CTT	ATT TAA I	CTT	TTT	GAT CTA D	• GGA CCT G	TTT	GTA CAT	AAA TTT	CAG
ACT TGA	GTT CAA	TGA	CTA GAT	AAA TTT K	TCT	• GAA CTT	ATT TAA I	CTT E 550	TTT	GAT CTA	GGA CCT G	TTT	GTA CAT	AAA TTT	CAG V>
ACT TGA T	GTT CAA V 630	TGA T	CTA GAT L	AAA TTT K	TCT R 40	GAA CTT E	ATT TAA I	CTT E 550	TTT	GAT CTA D	GGA CCT G	TTT	GTA CAT V	AAA TTT K	CAG V>
ACT TGA T	GTT CAA V 630	TGA T	CTA GAT L	AAA TTT K 64	TCT R 40 • GCA	GAA CTT E	ATT TAA I TCT	CTT E 550 AAC	TTT K	GAT CTA D	GGA CCT G 660	TTT K GGT	GTA CAT V	AAA TTT K 67	CAG V> 70 • GAA
ACT TGA T TTT	GTT CAA V 630	TGA T AAT TTA	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 40 • GCA CGT	GAA CTT E GGT CCA	ATT TAA I TCT AGA	CTT E 550 AAC TTG	TTT K AAA TTT	GAT CTA D	GGA CCT G 660 ACA TGT	TTT K GGT CCA	GTA CAT V  AAA TIT	AAA TTT K 67 TGG ACC	CAG V> 70 GAA CTT
ACT TGA T TTT	GTT CAA V 630	TGA T	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 40 • GCA CGT	GAA CTT E GGT CCA	ATT TAA I TCT AGA	CTT E 550 AAC TTG	TTT K	GAT CTA D	GGA CCT G 660 ACA TGT	TTT K GGT CCA	GTA CAT V  AAA TIT	AAA TTT K 67	CAG V> 70 GAA CTT
ACT TGA T TTT	GTT CAA V 630 TTG AAC L	TGA T AAT TTA N	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 40 • GCA CGT A	GAA CTT E GGT CCA	ATT TAA I TCT AGA	CTT E 550 AAC TTG N	TTT K AAA TTT K	GAT CTA D	GGA CCT G 660 ACA TGT T	TTT K GGT CCA G	GTA CAT V  AAA TIT	AAA TTT K 67 TGG ACC W	CAG V> 70 GAA CTT E>
ACT TGA T TTT	GTT CAA V 630 TTG AAC L	TGA T AAT TTA	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 40 • GCA CGT	GAA CTT E GGT CCA	ATT TAA I TCT AGA	CTT E 550 AAC TTG N	TTT K AAA TTT	GAT CTA D	GGA CCT G 660 ACA TGT T	TTT K GGT CCA	GTA CAT V  AAA TIT	AAA TTT K 67 TGG ACC W	CAG V> 70 GAA CTT
ACT TGA T	GTT CAA V 630 TTG AAC L	TGA T AAT TTA N	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA T	TCT R 40 GCA CGT A 690	GAA CTT E GGT CCA G	ATT TAA I TCT AGA S	CTT E 550 AAC TTG N	AAA TTT K	GAT CTA D • AAA TTT K	GGA CCT G 660 ACA TGT T	GGT CCA G	GTA CAT V AAA TTT K	AAA TTT K 67 TGG ACC W	CAG V> 70 GAA CTT E>
ACT TGA T TTT AAA F	GTT CAA V 630 . TTG AAC L	TGA T  AAT TTA N  680 ACT	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T	TCT R 40 GCA CGT A 690	GAA CTT E GGT CCA G	ATT TAA I TCT AGA S	E 550 AAC TTG N 70	AAA TTT K	GAT CTA D AAA TTT K	GGA CCT G 660 ACA TGT T	GGT CCA G	GTA CAT V  AAA TTT K	AAA TTT K 67 TGG ACC W	CAG V>  70 GAA CTT E>  720 AAA
ACT TGA T TTT AAA F	GTT CAA V 630 TTG AAC L	TGA T  AAT TTA N  680 ACT TGA	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T ACT TGA	TCT R 40 GCA CGT A 690 TTA AAT	GAA CTT E  GGT CCA G ACA TGT	ATT TAA I TCT AGA S ATT TAA	CTT E 550 AAC TTG N 70 AGT TCA	AAA TTT K GCT CGA	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	GGT CCA G	GTA CAT V  AAA TIT K  AAA TIT	AAA TTT K 67 TGG ACC W ACT TGA	CAG V> 70 GAA CTT E> 720 AAA TTT
ACT TGA T TTT AAA F	GTT CAA V 630 . TTG AAC L	TGA T  AAT TTA N  680 ACT TGA	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T ACT TGA	TCT R 40 GCA CGT A 690	GAA CTT E  GGT CCA G ACA TGT	ATT TAA I TCT AGA S ATT TAA	CTT E 550 AAC TTG N 70 AGT TCA	AAA TTT K	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	GGT CCA G	GTA CAT V  AAA TIT K  AAA TIT	AAA TTT K 67 TGG ACC W	CAG V> 70 GAA CTT E> 720 AAA TTT
ACT TGA T TTT AAA F	GTT CAA V 630 TTG AAC L	TGA T AAT TTA N 680 ACT TGA T	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T ACT TGA	TCT R 40 GCA CGT A 690 TTA AAT L	GAA CTT E GGT CCA G	ATT TAA I TCT AGA S ATT TAA	CTT E 550 AAC TTG N 70 AGT TCA	AAA TTT K OO • GCT CGA A	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	GGT CCA G 710 AAA TTT K	GTA CAT V  AAA TTT K  AAA TTT K	AAA TTT K 67 TGG ACC W ACT TGA	CAG V> 70 GAA CTT E> 720 AAA TTT
ACT TGA T TTT AAA F	GTT CAA V 630 TTG AAC L	TGA T AAT TTA N 680 ACT TGA T	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T ACT TGA	TCT R 40 GCA CGT A 690 TTA AAT L	GAA CTT E  GGT CCA G ACA TGT	ATT TAA I TCT AGA S ATT TAA	CTT E 550 AAC TTG N 70 AGT TCA	AAA TTT K GCT CGA	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	GGT CCA G 710 AAA TTT K	GTA CAT V  AAA TIT K  AAA TIT	AAA TTT K 67 TGG ACC W ACT TGA	CAG V> 70 GAA CTT E> 720 AAA TTT
ACT TGA T TTT AAA F GAC CTG	GTT CAA V 630 TTG AAC L AGT TCA S	AAT TTA N 680 ACT TGA T	CTA GAT L GAC CTG D AGC TCG S	AAA TTT K 64 ACT TGA T ACT TGA T	TCT R 40 GCA CGT A 690 TTA AAT L	GAA CTIT E GGT CCA G	ATT TAA I TAA I	CTT E 550 AAC TTG N 70 AGT TCA S	AAA TTT K OO • GCT CGA A	GAT CTA D AAA TTT K GAC CTG D	GGA CCT G 660 ACA TGT T	GGT CCA G 710 AAA TTT K	GTA CAT V . AAA TIT K . AAA TIT K	AAA TTT K 67 TGG ACC W ACT TGA T	CAG V> 70 GAA CTT E> 720 AAA TTT K>
ACT TGA T TTT AAA F GAC CTG D	GTT CAA V 630 . TTG AAC L AGT TCA S	AAT TTA N 680 ACT TGA T GTG	CTA GAT L GAC CTG D AGC TCG S TTC	AAA TTT K 64 ACT TGA T ACT TGA T TTA	TCT R 10 GCA CGT A 690 TTA AAT L	GAA CTIT E GGT CCA G ACA TGT T	ATT TAA I GGT	CTT E 50 AAC TTG N 70 AGT TCA S	AAA TTT K OO GCT CGA A 750	GAT CTA D AAA TTT K GAC CTG D	GGA CCT G 660 ACA TGT T AGC TCG S	GGT CCA G 710 AAA TTT K 7 CAA	GTA CAT V . AAA TIT K . AAA TIT K . CAA	AAA TTT K 67 TGG ACC W ACT TGA T	CAG V> 70 GAA CTT E> 720 AAA TTT K>
ACT TGA T TTT AAA F GAC CTG D	GTT CAA V 630 . TTG AAC L AGT TCA S	AAT TTA N 680 ACT TGA T 7 GTG CAC	GAC CTG D AGC TCG S TTC AAG	AAA TTT K 64 ACT TGA T ACT TGA T TTA	TCT R 40 GCA CGT A 690 TTA AAT L	GAA CTIT E GGT CCA G ACA TGT T	ATT TAA I TAA I GGT CCA	CTT E 550 AAC TTG N 70 AGT TCA S ACA TGT	AAA TTT K GCT CGA A 750	GAT CTA D AAA TTT K GAC CTG D	GGA CCT G 660 ACA TGT T AGC TCG S	GGT CCA G 710 AAA TTT K 7 CAA GTT	GTA CAT V . AAA TIT K . AAA TIT K . CAA	AAA TTT K 67 TGG ACC W ACT TGA T	CAG V> 70 GAA CTT E> 720 AAA TTT K>

Osp b/ fla (122-234) osp c 790 800 810 780 770 • • • ACA GCT GGA ACC AGC CTA GAA GGA TCA GCA AGT GAA ATT AAA AAT CTT TGT CGA CCT TGG TCG GAT CTT CCT AGT CGT TCA CTT TAA TTT TTA GAA TAGTSLEGSASEIKNL> 850 840 830 820 TCA GAG CTT AAA AAC GCT TTA AAA GGT CAC CCC ATG GGA AAT AAT TCA AGT CTC GAA TTT TTG CGA AAT TTT CCA GTG GGG TAC CCT TTA TTA AGT S E L K N A L K G H P M G K N S>

870 880 890 900 910

GGG AAA GAT GGG AAT ACA TCT GCA AAT TCT GCT GAT GAG TCT GTT AAA

GGG AAA GAT GGG AAT ACA TCT GCA AAT TCT GCT GAT GAG ICI GIT AAA
CCC TTT CTA CCC TTA TGT AGA CGT TTA AGA CGA CTA CTC AGA CAA TTT
G K D G N T S A N S A D E S V K>

920 930 940 950 960

GGG CCT AAT CTT ACA GAA ATA AGT AAA AAA ATT ACG GAT TCT AAT GCG
CCC GGA TTA GAA TGT CTT TAT TCA TTT TTA TGC CTA AGA TTA CGC
G P N L T E I S K K I T D S N A>

970 980 990 1000

GTT TTA CTT GCT GTG AAA GAG GTT GAA GCG TTG CTG TCA TCT ATA GAT CAA AAT GAA CGA CAC TTT CTC CAA CTT CGC AAC GAC AGT AGA TAT CTA V L L A V K E V E A L L S S I D>

1010 1020 1030 1040 1050

GAA ATT GCT GCT AAA GCT ATT GGT AAA AAA ATA CAC CAA AAT AAT GGT CTT TAA CGA CGA TTT CGA TAA CCA TTT TTT TAT GTG GTT TTA TTA CCA E I A A K A I G K K I H Q N N G>

1060 1070 1080 1090 1100

TTG GAT ACC GAA TAT AAT CAC AAT GGA TCA TTG TTA GCG GGA CGT TAT AAC CTA TGG CTT ATA TTA GTG TTA CCT AGT AAC AAT CGC CCT GCA ATA L D T E Y N H N G S L L A G R Y>

1110 1120 1130 1140 1150

GCA ATA TCA ACC CTA ATA AAA CAA AAA TTA GAT GGA TTG AAA AAT GAA CGT TAT AGT TGG GAT TAT TTT GTT TTT AAT CTA CCT AAC TTT TTA CTT A I S T L I K Q K L D G L K N E>

Osp b/ fla (122-234) osp c 1170 1170 1190 1180 1160 • . • GGA TTA AAG GAA AAA ATT GAT GCG GCT AAG AAA TGT TCT GAA ACA TTT CCT AAT TTC CTT TTT TAA CTA CGC CGA TTC TTT ACA AGA CTT TGT AAA G L K E K I D A A K K C S E T F> 1220 1230 1240 1210 ACT AAT AAA TTA AAA GAA AAA CAC ACA GAT CTT GGT AAA GAA GGT GTT TGA TTA TTT AAT TTT CTT TTT GTG TGT CTA-GAA-CCA TTT CTT CCA CAA TNKLKEKHTDLGKEG.V>. 1270 1280 1260 ACT GAT GCT GAT GCA AAA GAA GCC ATT TTA AAA ACA AAT GGT ACT AAA TGA CTA CGA CTA CGT TTT CTT CGG TAA AAT TTT TGT TTA CCA TGA TTT T D A D A K E A I L K T N G T K> 1310 1320 1330 1300 ACT AAA GGT GCT GAA GAA CTT GGA AAA TTA TTT GAA TCA GTA GAG GTC TGA TTT CCA CGA CTT CTT GAA CCT TTT AAT AAA CTT AGT CAT CTC CAG TKGAEELGKLFESVEV> 1360 1370 1380 • TTG TCA AAA GCA GCT AAA GAG ATG CTT GCT AAT TCA GTT AAA GAG CTT AAC AGT TTT CGT CGA TTT CTC TAC GAA CGA TTA AGT CAA TTT CTC GAA L S K A A K E M L A N S V K E L> 1420 1400 1410 1430 ACA AGC CCT GTT GTG GCA GAA AGT CCA AAA AAA CCT GGT ACC ATG GCT TGT TCG GGA CAA CAC CGT CTT TCA GGT TTT TTT GGA CCA TGG TAC CGA T S P V V A E S P K K P G T M A> 1460 1470 1480 CAA TAT AAC CAA ATG CAC ATG TTA TCA AAC AAA TCT GCT TCT CAA AAT GTT ATA TTG GTT TAC GTG TAC AAT AGT TTG TTT AGA CGA AGA GTT TTA Q Y N Q M H M L S N K S A S Q N> 1510 1520 1530 1500 GTA AGA ACA GCT GAA GAG CTT GGA ATG CAG CCT GCA AAA ATT AAC ACA CAT TCT TGT CGA CTT CTC GAA CCT TAC GTC GGA CGT TTT TAA TTG TGT V R T A E E L G M Q P A K I N T>

Osp b/ fla (122-234) osp c 1550 1560 1570 CCA GCA TCA CTT TCA GGG CTT CAA GCG TCT TGG ACT TTA AGA GTT CAT GGT CGT AGT GAA AGT CCC GAA GTT CGC AGA ACC TGA AAT TCT CAA GTA PASLSGLQASWTLRVH> 1600 1610 1590 1620 GTT GGA GCA ACC CAA GAT GAA GCT ATT GCT GTA AAT ATT TAT GCA GCT CAA CCT CGT TGG GTT CTA CTT CGA TAA CGA CAT TTA TAA ATA CGT CGA V G A T Q D E A I A V N I Y A A> 1650 1660 1650 1670 1640 AAT GTT GCA AAT CTT TTC TCT GGT GAG GGA GCT CAA ACT GCT CAG GCT TTA CAA CGT TTA GAA AAG AGA CCA CTC CCT CGA GTT TGA CGA GTC CGA N V A N L F S G E G A Q T A Q A> 1720 1710 1690 1700 GCA CCG GTT CAA GAG GGT GTT CAA CAG GAA GGA GCT CAA CAG CCA GCA CGT GGC CAA GTT CTC CCA CAA GTT GTC CTT CCT CGA GTT GTC GGT CGT A P V Q E G V Q Q E G A Q Q P A> 1740 1750 1760 CCT GCT ACA GCA CCT TCT CAA GGC GGA GTT GGT CAC C GGA CGA TGT CGT GGA AGA GTT CCG CCT CAA CCA GTG G PATAPSQGGVGHX>

			1	10			20			30		*	4	10	•	
OspC-B31	ATG TAC	* AAA TTT		*		TT D	ACT	GCG	מידמ	<b>ጥጥ</b> A	ATG	ACT	TTA	TTT AAA	TTA AAT	TTT AAA
					•••											
[ 1832 ]	•••	• • •	•••	•••	•••	•••	•••	•••	• • •	•••	•••					
2. OspC-T	R •••	•••	•••		•••	•••	20	•••	•••		•••	•••	••••	•••	•••	>
3. OspC-K	4	•••		10			20	• • •		30			•••	10	• • •	>
•											80			00		•
	*		*	*		*	CCC	*	* CDT	GGG	*	ACA	* TCT	GCA	AAT	* TCT
	TAT	AGA	ACA	TTA	TTA	AGT	ccc	TTT	CTA	CCC	TTA	tgc	MGA	CGI	IIN	NON
1. OspC-P. [ 1832 ]	K50	•••	•••	60	•••	•••	•••	70	.g.		80 g	ţ	90	a.t	•••	c>
2. OspC-T	R50			60			t	70 aga			tc.	80 g	•••	a.t		00
3 OccY	450	•••	•••	60	•••	•••		70 70				80			9	90
3. OspC-K [ 1774 ]	***	•••	•••	•••	•••	•••	t	999	• • •		.cc	g	• • •	a.t		>
•	1	00			110			120		*	1	30	*		140	
OspC-B31	GCT CGA	GAT CTA	GAG CTC	TOT	ርጥጥ	222	ccc	CCT	AAT	CTT	ACA	GAA CTT	ATA	AGT	AAA TTT	AAA TTT
1. OspC-1 [ 1832 ]	00	c		110	.cg	•••	120		•••		30		•••	140 c		>
2. OspC-T																
3 0e2C=K	·A	•••	1	nn			110			120			1	30		
3. OspC-K [ 1774 ]		•••	•••	•••	.ca	•••	a	•••	•••	•••	• • •	.t.	•••	с	•••	>
		150		4	1	60			170			180		*	19	90
OspC-B31	ATT	י ארכ	CDT	ጥርፕ	דממ י	GCG	GTT	TTA	CTT	GCT	GTG	AAA	GAG	GTT	GAA	GCG
1. OspC-F																
1. OspC-F [ 1832 ]	•••	a	• • •	•••	• • •	a	t	g	•••	•••	t	• • • •	a			a.t>
2. OspC-1 [ 1786 ]												•••				t>
3. OspC-F	140	a	٠	150	• • • •	a	t	g.,	9	• • • •	170	•••	a	180	g	t>
			200			210	)			20			230			240
OspC-B31	TTC	CTC	*	TC	* የጥል ግ	r Cad	r Gaz	* ATI	CCI	* GCI	AAA	GCT	* ATI	GGT	* ' AAA ''''''	AAA TTT
1 0000			; AGI	r AGI	210		CTI		1 CGP 220	CGP		230	IAA	CUA	240	TTT
1. OspC-I [ 1832 ]	•••	g.t	.t.	• • •		• • • •	• • •	. с.	• • • •	aag	,		• • •	• • •		
2. OspC-7	rr i	190			200			210	) 	<b></b> .	• • • •		20	• • •		230 >

Figure 38 (1 of 3)

1	3. OspC-K	4 19	0 a.c	•••	2	00	•••	• • •	210 c		aa.		0	•••	2	30	gt.>
				25	0		2	60 .		*	270		*.	28	<b>O</b>	*	
	spC-B31	TAT	GTG	CAA	AAT TTA	AAT TTA	GGT CCA	TTG AAC	GAT CTA	ACC TGG	GAA CTT	TAT ATA	AAT TTA	CAC GTG	TTA	GGA CCT	TCA AGT
,	1. OspC-P.	ĸ	25	50 a.t		2	60	a	.c.	270 g.t	tt.	a	28	g		2	:90 ••g>
							tạc										
	2. OspC-T	R			240		25	0		. 2	260			270	_	•	·
I	1786 ]	•••			•••	g	•••	a	•••	.a.	•••	gca	•••	.ga			
ſ	3. OspC-K 1774 ]	4	240 t	•••	•••			a	a	g.t	a.t	gcg	gg •	a	с		>
		290			300			31	ιŌ	_	:	320			330		•
O	spC-B31	TTG AAC	TTA AAT	¢ GCG CGC	GGA CCT	CGT GCA	TAT ATA	GCA CGT	ATA TAT	TCA AGT	ACC TGG	CTA GAT	ATA TAT	AAA TTT	CAA GTT	AAA TTT	TTA AAT
f	1. OspC-P 1832 ]	ĸ		300		acc	31	10			320			330 .c.	g		g>
	2. OspC-2 1786 ]																
I	3. OspC-K 1774 ]		•••	290 a		gcc	300	••••	•••		10	• • •		320 .c.	g	•••	330
		, 3	40		:	350			360			31	70		3	380	
	spC-B31	CTA	GGA CCT	TTG AAC	AAA TTT	AAT TTA ttt	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT	TAA	GAT CTA	CGC	# GCT CGA	110
	anCB31	GAT CTA	GGA CCT	TTG AAC	AAA TTT	AAT TTA ttt	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT	TAA	GAT CTA	CGC	# GCT CGA	110
(	1. OspC-3	GAT CTA 340 ag.	GGA CCT	TTG AAC	AAA TTT 350	AAT TTA ttt	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT	ATT	GAT CTA 380 .ca	GCG CGC	GCT CGA	390
(	spC-B31	GAT CTA 340 ag.	GGA CCT	TTG AAC	AAA TTT 350	AAT TTA ttt a 40 tca	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT	ATT	GAT CTA 380 .ca	GCG CGC	GCT CGA	390
[	1. OspC-3 1832 ] 2. OspC-1 1786 ]	GAT CTA 340 ag. RR330 ag.	GGA CCT aa.	TTG AAC	AAA TTT 350	AAT TTA ttta	360 	.a.	TTA AAT  350	AAG TTC	GAA CTT 70 ac.	9 360	TAA	GAT CTA 380 .ca	aa. 3.	GCT CGA	390
[	1. OspC-3	GAT CTA 340 ag. RR330 ag.	GGA CCT aa.	TTG AAC	AAA TTT 350	AAT TTA ttta	360 	.a.	TTA AAT  350	AAG TTC	GAA CTT 70 ac.	9 360	TAA	GAT CTA 380 .ca	aa. 3.	GCT CGA	390
[	1. OspC-3 1832 ] 2. OspC-1 1786 ]	GAT CTA 840 ag. RR330 ag.	aat.	TTG AAC	350  36 	AAT TTA ttt 40 tca ttc	360 	.a.	350	3  360	GAA CTT 70 ac.	360 	TAA	GAT CTA 380 .ca a.a 70	aa. .a.	GCT CGA	390 > >
1	1. OspC-3 1832 ] 2. OspC-1 1786 ]	GAT CTA 340 ag. RR330 ag. (4 ag.	aat. aa. TGT	TCT AGA	AAA TTT 350 t 40 t	AAT TTA ttt a 40 tca ttc a ACA TGT	350 	.a. .a.	TTA AAT 350 	360  410 AAA	GAA CTT 70 ac. a	G 360 	TAA  3  420 GAA CTT	GAT CTA 380 .ca a.a 70 a	GCG CGC aa. 3. .a.	GCT CGA	390>> 380> 380>
1 1	1. OspC-3 1832 ] 2. OspC-7 1786 ] 3. OspC-1 1774 ]	GAT CTA 340 ag. R330 ag. 44 ag.	aa. .t. 390	TCT AGA	AAA TTT 350 t 40 t	AAT TTA ttt a 40 tca ttc a ACA TGT	350 	.a. .a.	TTA AAT 350 	360 t 410 AAA	GAA CTT 70 ac. a	G 360	ATT TAA   420  GAA CTT	GAT CTA 380 .ca a.a 70 a	aa. 3a.  CAC GTG	GCT CGA 70 4. ACA TGT	390>> 380> 30> GAT CTA
1 1	1. OspC-3 1832 ] 2. OspC-7 1786 ] 3. OspC-1 1774 ] spC-B31 1. OspC-1 1832 ]	GAT CTA 340 ag. RR330 ag. 4 ag.	aa. .t. 390 *TGT	TCT AGA	AAA TTT 350 t 40  GAA CTT	AAT TTA ttt a 40 tca ttc a ACA TGT ga.	GAA CTT 360 	.aa. ACT TGA	350	360  410 AAA	GAA CTT 70 ac. a TTA AAT 420	G 360	TAA  3  420  GAA CTT	GAT CTA 380 .ca a.a 70 a AAA TTT 4	aaa. cac gTG	GCT CGA 70  4 ACA TGT	390>> 380> 30 * GAT CTA>
1 0	1. OspC-3 1832 ] 2. OspC-7 1786 ] 3. OspC-1 1774 ]	GAT CTA 340 ag. rR330 ag. 4 ag. TTT	aa. .t. aa. 390 * ACA	TCT AGA	AAA TTT 350 t 40 t	AATTTA TTTA ttt a 40 tca ttc a ACA TGT ga. 390	360 350 TITA	.aag ACT TGA	TTA AAT 350 	360 360 410 AAA TTT	GAA CTT 70 ac. a TTA AAT 420	G 360	ATT TAA  3 420 GAA CTT agt	GAT CTA 380 .ca a.a 70 a AAA TTT 40	aaaa. cac grg	GCT CGA	390>> 380> GAT CTA>
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1. OspC-3 1832 ] 2. OspC-1 1786 ] 3. OspC-1 1774 ] spC-B31 1. OspC-1 1832 ] 2. OspC-2	GAT CTA 340 ag. R330 ag. 44 ag. TTT PK 	aa. .t. 390 TGT ACA	TCT AGA	AAA TTT 350 t 40 	AATTTA ttta 40 tca ttca 4 ACA TGT ga. 390 .a.	360 350 TTT AAA	.aag ACT TGA	AAT AAT TTA AAC.	360  360 t 410 AAA TTT	GAA CTT 70 ac. a TTA 420 c	G 360	ATT TAA   420 GAA CTT  agt 410t	GAT CTA 380 .ca a.a 70 a AAA TTT 4ggt	aaa. cAC GTG 30 .t	GCT CGA 70  4 ACA TGT 9	390>> 380> 30> GAT CTA>

Figure 38 (2 of 3)

_	CTT GG	A TTT	CTT	CCA	CAA	TGA	CTA	CGA	CTA	CGT	TTT	CIT	CGG	TAA	MAT
1. OspC-P [ 1832 ]															
2. OspC-T	R	130 t.	C	a.c	<b>140</b>	cag	•••	450 .a.	a	•••		50 a	t	•••	470 >
3. OspC-4 [ 1774 ]															
		4	90		:	500			510			5	20		
OspC-B31	AAA AC	יית מ	CCT	D COLD	DDD	D CTT	AAA	GGT	GCT	GAA	GAA	CTT	GGA	MMM	TIA
1. OspC-P [ 1832 ]	K 490			500			510			52	20	•		530	. 5
2. OspC-T [ 1786 ]	ж	480 . c	a	• • •	4:	gac	g	•••	•••	a	• • •	•••	.a.	g.g	>
3. OspC-K	4480		49	90		!	500_			510	_		52	20	_
[ 1774 ]	g t.	• • • •	cc.	•••	•••	ga.	g	•••	•••	<b>d</b>		•••	aa.	y.c	•••
	530 *	_	540		_	5	50			60			570		
OspC-B31	TTT GA AAA CT	A TCA	GTA	GAG	GTC	TTG	TCA	AAA	GCA	GCT	AAA	GAG	ATG	CTT	GCT CGA
1. OspC-P [ 1832 ]	K 54	0		5	50			560			570	ta	aca	50 . a	80 a>
Z. UBPC-5			~ 411			540			5.	,,		•	300		
2. OspC-5 [ 1786 ]	a.	• • • •	с	a	ag.	• • •	• • •	• • •	• • •	g	с	.ca	gca	t.a	a
[ 1786 ] 3. OspC-K [ 1774 ]															
	4 530 .c		•••	540 a	ag.	•••	g	50	•••	g	60 c	a	gca	570 t.a	
	580	• • • • * A GTT	 !	540 a 590 *	ag.	* ACA	5: g 600 *	CCT	* GTT	g 6: GTG	560 C 10 *	a *	gca	570 t.a 620 *	>
3. OspC-K [ 1774 ] OspC-B31	580 580 AAT TC	 * A GTT T CAA	AAA TTT	540 a 590 * GAG CTC	ag. CTT GAA	* ACA	g 600 * AGC TCG	CCT GGA	* GTT CAA	GTG CAC	GCA CGT	a * GAA CTT	gca AGT TCA	570 t.a 620 * CCA GGT	AAA TTT
3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ]	580 580 TTA AG	A GTT T CAA 590	AAA TTT	540 a 590 * GAG CTC	ag. CTT GAA 600	* ACA TGT	g 600 * AGC TCG	CCT GGA	GTT CAA	6: GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 620 * CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ] OspC-B31	580 580 TTA AG	A GTT T CAA 590	AAA TTT	540 a 590 * GAG CTC	ag. CTT GAA 600	* ACA TGT	g 600 * AGC TCG	CCT GGA	GTT CAA	6: GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 620 * CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ]	580 AAT TC TTA AG	* * * * * * * * * * * * * * * * * * *	AAA TTT	540 a 590 GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA 10	6: GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 620 CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ] OspC-B31  1. OspC-P [ 1832 ] 2. OspC-T [ 1786 ]	580 580 AAT TC TTA AG  OK  CR570	* A GTT CAA 590	AAA TTT	540 a 590 GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA 10	6: GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 620 CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ] OspC-B31  1. OspC-P [ 1832 ] 2. OspC-T [ 1786 ]	580 AAT TC TTA AG	A GTT CAA 590	AAA TTT	540 a 590 GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA 10	6: GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 620 CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ]  OspC-B31  1. OspC-F [ 1832 ]  2. OspC-T [ 1786 ]  3. OspC-K [ 1774 ]	580 AAT TC TTA AG CR CR570 AAA CC TTT GG	A GTT CAA 590	AAA TTT	540 a 590 GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA 10	6: GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 620 CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P [ 1832 ]  2. OspC-T [ 1786 ]  3. OspC-K [ 1774 ]  OspC-B31  1. OspC-F	580 AAT TC TTA AG  CR570 AAAA CC TTT GG	A GTT CAA 590	AAA TTT	540 a 590 GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA 10	6: GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 620 CCA GGT	AAA TTT 630

				•				_	, .							
								95	1/13	33						
			10	)			20		*	30		*	. 4	0		
BO ospD	CTA (	* ~~~ *	ו ג מידייו				מיתית	TOTAL CO.	CTC	TEA	ATA	TCT	TGT	TCT	TTA	GAT
во овър	GAT (	GAC I	AAT :	CA I	AAT A	AAA	AAT	AAC	GAG	AGT	TAT	AGA	ACA	AGA	AAT	CTA
1 B-Cau (	_		10	)			20			30			4	0		_
1. P-Gau ( [ 2804 ]	•••	• • •	• • •	• • •	•••	• • •	• • •	• • •	•••	•••	•••	• • •	• • •	.a.	•••	•••>
2. DK29 o	8		10	0			20			30				0		
2. DK29 of [ 2786 ]	•••	(	c	• • •	• • •	• • •	• • •	• • •	• • •	•••	•••	• • •	g	•••	• • •	>
3. K48 os	D		10	0			20			30			4	0		
3. K48 os	• • •	• • •	• • •	• • •	•••	• • •	• • •	• • •	•••	•••	• • •	•••	•••	• • •	•••	
							_				90			90		
	50 *		*	60 *		*	7	*	*		*		*	*		*
BO ospD	AAT TTA	GAA	GGT	GTA .	AAC	TCA	AAA	GAT	TAC	GAG	TCA	AAA	AAA	CAG	AGT	ATA TAT
	TTA	CTT	CCA	CAT	TTG .	AGT	111	CIA	AIG	CIC	71.01				•	
1. P-Gau	o50			60			•	70			80			90		>
[ 2804 ]	•••	• • •	• • •	• • •	• • •	• • •			•••	•••						
2. DK29 o [ 2786 ]	s50			60				70			80			90		>
-																
3. K48 os	p50			60	α.			70			80			90		>
[ 2786 ]	•••	•••	•••	•••	•9•		• • •									
	10	00		1	.10			120			1:	30		:	140	
BO ospD						anc	*	* *	ccc	*	ልሮተ	*	* AAT	TCA	*	AAA
BO ospD	CTA GAT	CCA	CTT	AAT	TTA	GTC	GAT	AAC	CCC	GTT	TGA	TGT	TTA	AGT	GAT	TTT
1. P-Gau								120				30			140	
[ 2804 ]	•••	• • •		•••	•••			•••	• • •	• • •	• • •	• • •	• • •	• • •	•••	>
2. DK29 C	sa 16	20		1	110			120			1	30			140	
[ 2786 ]		• • •		•••	•••	• • •	• • •		• • •	• • •	• • •	• • •	• • •	• • •	• • •	>
3. K48 os	n 10	00		1	110			120	)		1	30			140	
[ 2786 ]	••••	•••	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	•••	• • •	• • •	• • •	>
																00
		150 *		*	16	50 *	*	,	170		*	180		*	1	*
BO ospD	GAA	CCB	222	דממ	ACA	ACA	GAT	' AAT	TTA	CAA	. GCA	TCA	TAA	GAG	GCA	AAT
	CTT	CGT	TTT	TTA	TGT	TGT	CTA	1 TTA	AAT	TIM	CGI	AGI	110			TTA
1. P-Gau	0	150			10	50			170			180				>
[ 2804 ]	• • •															
2. DK29 ( [ 2786 ]	os	150			10	50			170			180	)			190 >
_																
3. K48 of	вр	150			10	60			170			180				L90 >
[ 2/86 ]	•••	•••	•••	•••	•••	•••		- ••	<b>.</b>							
			200			210	)		2	220			230			240
	*				*	*		*	2	*	• • • •		. *	, mar		י הכתר יים בתי
BO ospD	AAA TTT	GTT CAA	GTA CAT	GAA CTT	GCA CGT	CAP	TA'	n AG	A CAC	CAI	A TT	AA?	TAT 1	AGI	r AG	r gct A cga

				96	133		
1 P-Gau O	200		210	2	20	230	240
1. P-Gau o							
2. DK29 ов [ 2786 ]	200		210	. 23	20	230	240
						• • • • • •	>
3. K48 osp [ 2786 ]	200		210		20	230	240
,	21	:n	260		270	28	10
	*	* *	*	*	*	*	80 * * .
BO ospD GCA	GAT CAG CTA GTC	GTA AAA CAT TTT	GGT CAA CCA GTT	CAA CAA GTT GTT	ATA TGC TAT ACG	ACG ATT TGC TAA	TAG CTC AAA ATC GAG TTT
1. P-Gau o	2	50	260		270	28	30
1. P-Gau o	•••	• • • • • •	•••	•••	• • • • • •	•••	>
2. DK29 os	29	50	260		270	28	30
2. DK29 os [ 2786 ]	•••	g	••••	• • • • • •	• • • • • • • • • • • • • • • • • • • •	•••	>
3. K48 osp [ 2786 ]	•••	g		•••			>
290 * BO OSPD TGG ACC	•	300	3:	10	320	*	330
BO OSPD TGG	CAG AAA	TAG ATT	TAG AAA	AAA TAA	AGG AAT	CTA GTG	ATA AAG TAA
ACC	GTC TTT	ATC TAA	ATC TTT	TTT ATT	TCC TTA	GAT CAC	TAT TTC ATT
1. P-Gau 290		300	3:	10	320		330
[ 2804 ]	• • • • • • • • • • • • • • • • • • • •	• • • • • • •	• • • • • • •	•••	•••	• • • • • •	>
2. DK29 o290 [ 2786 ]		300	3:	10	320		330
[ 2786 ]	•••	•••	•••	•••	• • • • • •	•••	>
3. K48 os290		300	3:	10	320		330
[ 2786 ]	• • • • • • • • • • • • • • • • • • • •	•••	•••	•••	•••	• • • • • •	>
3	40	350 *		360	37	70	380
BO ospD TAG							
ATC	AAC GCC	GAT TAC	AAC GCT	TTC TTC	GTA TAT	TGG AAT	GAT TTC GTC
1. P-Gau o 3	40	350		360	3.	70	380
[ 2804 ]			• • • • • •		•••	•••	
2. DK29 os 3	40	350		360	3'	70	380
[ 2786 ]					•••		
3. К48 овр 3	40	350		360	3.	70	380
[ 2786 ]				•••			
	390 *	4	00	410	•	420 *	430 * *
BO ospD TAG		ATA TGC	AAA AAC	TGT ACA	AAG AGC	AAG AAG	AGC AAC TAA
ATC	TTG TTT	TAT ACG	TTT TTG	ACA TGT	TTC TCG	TTC TTC	TCG TTG ATT
1. P-Gau o	390	4	00	410		420	430
[ 2804 ]							
2. DK29 os							

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									9	7 <i>113</i>	?3						
[ :	2786 ]	• • • •	•••	• • •	•••	•••	•••	• • •	•••	•••	•••	•••	•••	•••	•••		>
	3. K48 os 2786 ]	p	390			40	00			410		•••	420	•••	•••	4:	30
		•		440 *		*	450		*	4	50 *	*		470 *		*	480
ВО	ospD	AAC TTG				TTC	TGA	TGA	AAC	AGA	ACG	AGT	TTC	TGA	TGA		
	1. P-Gau 2804 ]				•••	•••	450 •••		•••			•••		470 •••	•••	•••	480 >
[ 2	2. DK29 o 2786 ]	s ••••	•••	440	• • •	•••	450 •••		.g.	40	50	•••	•••	470 •••	•••	•••	480 >
	3. К48 ов	P		440			450			40	50			470			480
[ 2	2786 ]	•••	• • •	•••	•••	•••	•••	•••	·g·	•••	•••	•••	•••	•••	•••	•••	···>
			*	49	90	*		500		*	510		*	52	20	*	
ВО	Ogeo	ACA TGT	AGC TCG	TAA	AGA	GGC	TGT	AGA	AAT	AGC	TTG	GAA	AGC	CAC	AGT	AAA	AGT
( 2	1. P-Gau 2804 ]	•		49	90	•••			•••	•••	510	•••	•••	52	20	•••	>
[ 2	2. DK29 o 2786 ]	• • •	• • •	• • •	•••	• • •	•••	• • •	• • •	• • •	•••	• • •	• • •		• • •		
[ 2	3. K48 os 2786 ]	P 	• • •	49	90	•••			•••	•••	510	•••	• • •		20	•••	>
		530 *		*	540 *		*	5!	50	*	!	560		*	570		
ВО	OgpD	AAA TTT	AGA	TGA	GTT	AAT	TGA	TGT	AGA	AAA	TGC	AGT	CAA	AGA	GGC	ATT	GGA
[ 2	l. P-Gau ! 2804 }	530	• • •	• • •	540			5!	50	•••		560		•••	570		>
2	2. DK29 o	530			540			5!	50			560			570		
[ 2	2786 ]	• • •	• • •	•••	•••					•••	•••	• • •	•••	•••	•••	•••	>
	3. K48 os: 2786 ]		• • •	•••	540			5!	50			560	•••	•••	570	•••	>
			30 *	*	5	90		*	600		*	61	10		•	520	
ВО	ospD	TAA ATT	AAT TTA	AAA		AGA	AAC	CGC	GAA	CAA	TAC	AAA	ACT	TAC	AGA	TAT	AGA TCT
	l. P-Gau ( 2804 ]			•••	•••	90	•••	•••	600		•••	61		•••		20	>
	2. DK29 o	s 58				90	•••	•••	600		•••	62	10	•••		20	>
3 [ 2	3. K48 os <sub>j</sub> 2786 j	p 58	30	•••		g	•••	•••	600		•••	61	10	•••		520	>

									9	8/1	<b>2</b> 3					
		630		*	64	*	*		550 *	•	*	660 *		*		*
BO ospD	aca.	AGT TCA	AGC TCG	AGA TCT	GTT CAA	AGT TCA	ATT TAA	aca Tgt	GAT CTA	AGC TCG	CAA GTT	AAA TTT	TGT ACA	AGC TCG	GGA CCT	TTA ATT
1. P-Gau	·	630		•••	64	10	•••		650 a	•••		660	•••	•••		70 >
2. DK29 o [ 2786 ]	s •••	630	•••	•••	64	40	•••	•••	650 a	•••	•••	660	•••		61	70 >
3. K48 os [ 2786 ]	p 	630	•••	•••	6	40	•••	•••	650 a	•••	•••	660	•••	•••		70 •••>
		f	680			690			7	00						
BO ospD	* AGC TCG	GCA CGT	* AGA TCT	AGT TCA	* TGT ACA	GGC CCG	CTT GAA	* GTT CAA	AAA TTT	* TAC ATG	TT AA					
1. P-Gau [ 2804 }	٥	•••	680	•••		690			7	00	>					
2. DK29 o [ 2786 ]	8	• • •	680	•••	•••	690		•••	7	00	>					
3. K48 os [ 2786 ]						690		•••	7	00	>					

P41 Sequence Range: 1 to 1011 10 20 ATG ATT ATC AAT CAT AAT ACA TCA GCT ATT AAT GCT TCA AGA AAT PAT TAC TAA TAG TTA GTA TTA TGT AGT CGA TAA TTA CGA AGT TCT TTA TTA Met Ile Ile Asn His Asn Thr Ser Ala Ile Asn Ala Ser Arg Asn Asn> 90 70 50 GGC ATT AAC GCT GCT AAT CTT AGT AAA ACT CAA GAA AAG CTT TCT AGT CCG TAA TTG CGA CGA TTA GAA TCA TTT...TGA GTT CTT TTC GAA AGA TCA Gly Ile Asn Ala Ala Asn Leu Ser Lys Thr Gln Glu Lys Leu Ser Ser> 130 120 110 100 GGC TAC AGA ATT AAT CGA GCT TCT GAT GAT GCT GCT GGC ATG GGA GTT CCG ATG TCT TAA TTA GCT CGA AGA CTA CTA CGA CGA CCG TAC CCT CAA Gly Tyr Arg Ile Asn Arg Ala Ser Asp Asp Ala Ala Gly Met Gly Val> 170 180 190 150 160 TCT GGT AAG ATT AAT GCT CAA ATA AGA GGT TTG TCA CAA GCT TCT AGA AGA CCA TTC TAA TTA CGA GTT TAT TCT CCA AAC AGT GTT CGA AGA TCT Ser Gly Lys Ile Asn Ala Gln Ile Arg Gly Leu Ser Gln Ala Ser Arg> 220 230 210 AAT ACT TCA AAG GCT ATT AAT TTT ATT CAG ACA ACA GAA GGG AAT TTA TTA TGA AGT TTC CGA TAA TTA AAA TAA GTC TGT TGT CTT CCC TTA AAT Asn Thr Ser Lys Ala Ile Asn Phe Ile Gln Thr Thr Glu Gly Asn Leu> 260 270 280 250 AAT GAA GTA GAA AAA GTC TTA GTA AGA ATG AAG GAA TTG GCA GTT CAA TTA CTT CAT CTT TTT CAG AAT CAT TCT TAC TTC CTT AAC CGT CAA GTT Asn Glu Val Glu Lys Val Leu Val Arg Met Lys Glu Leu Ala Val Gln> 320 300 310 290 TCA GGT AAC GGC ACA TAT TCA GAT GCA GAC AGA GGT TCT ATA CAA ATT AGT CCA TTG CCG TGT ATA AGT CTA CGT CTG TCT CCA AGA TAT GTT TAA Ser Gly Asn Gly Thr Tyr Ser Asp Ala Asp Arg Gly Ser Ile Gln Ile> 360 370 350 340 GAA ATA GAG CAA CTT ACA GAC GAA ATT AAT AGA ATT GCT GAT CAA GCT CTT TAT CTC GTT GAA TGT CTG CTT TAA TTA TCT TAA CGA CTA GTT CGA

Glu Ile Glu Gln Leu Thr Asp Glu Ile Asn Arg Ile Ala Asp Gln Ala>

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TTG	GTT	TAC	GTG	TAC	AAT .	AGT '	TTG	1-1-1	AGA	Ala	AGA	CIT	TTA	
Asn	GIN,	Met	HIS	Met	Leu	ser .	ASII	гÃ2	261	MIG	361	<b>6</b>	V211>	
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ACA	GCT	GAA	GAG	CTT	GGA	ATG	CAG	CCT	GCA	AAA	ATT	AAC	ACA	
TGT	CGA	CTT	CTC	GAA	CCT	TAC	GTC	GGA	CGT	TTT	TAA	TTG	TGT	
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Ser	Leu	Ser	Gly	Leu	Gln	Ala	Ser	Trp	Thr	Leu	Arg	Val	His>	
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CGT	TAA ATT	CTT GAA	AAG	AGA	GGT CCA	CTC	CCT	GCT CGA	• CAA GTT	TGA	GCT CGA	CAG GTC	CGA	
CGT	TAA ATT	CTT GAA	AAG	AGA	GGT CCA	CTC	CCT	GCT CGA	• CAA GTT	TGA	GCT CGA	CAG GTC		
CGT	TAA ATT	CTT GAA Leu	AAG	AGA	GGT CCA Gly	CTC	CCT	GCT CGA	• CAA GTT	TGA	GCT CGA	CAG GTC Gln	CGA	
CGT Ala	AAT TTA Asn	CTT GAA Leu	AAG Phe 40	AGA Ser	GGT CCA Gly	CTC Glu 550	CCT	GCT CGA Ala	CAA GTT Gln 660	TGA	GCT CGA Ala	CAG GTC Gln	CGA Ala>	
CGT Ala	AAT TTA Asn	CTT GAA Leu - 6	AAG Phe 40 GGT	AGA Ser	GGT CCA Gly	CTC Glu 550 CAG	CCT Gly GAA	GCT CGA Ala	CAA GTT Gln 660	TGA	GCT CGA Ala	CAG GTC Gln 6	CGA Ala> 70 • GCA	
CGT Ala GGTT CAA	AAT TTA Asn CAA GTT	CTT GAA Leu 6 GAG CTC	AAG Phe 40 GGT CCA	AGA Ser GTT CAA	GGT CCA Gly CAA GTT	CTC Glu 550 CAG GTC	CCT Gly GAA CTT	GCT CGA Ala * GGA CCT	CAA GTT Gln 660 GCT CGA	TGA Thr CAA GTT	GCT CGA Ala CAG	CAG GTC Gln 6 CCA GGT	CGA Ala> 70 • GCA CGT	
CGT Ala GGTT CAA	AAT TTA Asn CAA GTT	CTT GAA Leu 6 GAG CTC	AAG Phe 40 GGT CCA	AGA Ser GTT CAA	GGT CCA Gly CAA GTT	CTC Glu 550 CAG GTC	CCT Gly GAA CTT	GCT CGA Ala * GGA CCT	CAA GTT Gln 660 GCT CGA	TGA Thr CAA GTT	GCT CGA Ala CAG	CAG GTC Gln 6 CCA GGT	CGA Ala> 70 • GCA	
CGT Ala GGTT CAA Val	AAT TTA Asn CAA GTT	CTT GAA Leu 6 GAG CTC	AAG Phe 40 GGT CCA	AGA Ser GTT CAA	GGT CCA Gly CAA GTT	CTC Glu 550 CAG GTC Gln	CCT Gly GAA CTT	GCT CGA Ala * GGA CCT	CAA GTT Gln 660 GCT CGA	TGA Thr CAA GTT	GCT CGA Ala CAG	CAG GTC Gln 6 CCA GGT	CGA Ala> 70 • GCA CGT	
CGT Ala GGTT CAA	AAT TTA Asn CAA GTT	CTT GAA Leu 6 GAG CTC	AAG Phe 40 GGT CCA Gly	AGA Ser GTT CAA	GGT CCA Gly CAA GTT	CTC Glu 550 CAG GTC Gln	GAA CTT Glu	GCT CGA Ala * GGA CCT	CAA GTT Gln 660 GCT CGA Ala	TGA Thr CAA GTT Gln	GCT CGA Ala CAG	CAG GTC Gln 6 CCA GGT	CGA Ala> TO GCA CGT Ala>	
CGT Ala GGTT CAA Val 680	AAT TTA Asn CAA GTT Gln	CTT GAA Leu 6. GAG CTC Glu	AAG Phe 40 GGT CCA Gly 690	AGA Ser GTT CAA Val	GGT CCA Gly CAA GTT Gln	CTC Glu 550 CAG GTC Gln 70	GAA CTT Glu	GCT CGA Ala * GGA CCT Gly	CAA GTT Gln 660 GCT CGA Ala	TGA Thr CAA GTT Gln 710 CCT	GCT CGA Ala CAG GTC Gln	CAG GTC GIn CCA GGT Pro	CGA Ala> 70 GCA CGT Ala> 720 GTT	
GGTTCAA	AAT TTA Asn CAA GTT Gln	CTT GAA Leu GAG CTC Glu CCT GGA	AAG Phe 40 GGT CCA Gly 690 TCT AGA	AGA Ser GTT CAA Val	GGT CCA Gly CAA GTT Gln	CTC Glu 550 CAG GTC Gln 70 GGA CCT	GAA CTT Glu OO GTT	GCT CGA Ala GGA CCT Gly AAT	CAA GTT Gln 660 GCT CGA Ala	TGA Thr CAA GTT Gln 710 CCT GGA	GCT CGA Ala CAG GTC Gln	CAG GTC GIn CCA GGT Pro	CGA Ala> TO GCA CGT Ala> TZE GTT CAA	
GGTTCAA	AAT TTA Asn CAA GTT Gln	CTT GAA Leu GAG CTC Glu CCT GGA	AAG Phe 40 GGT CCA Gly 690 TCT AGA	AGA Ser GTT CAA Val	GGT CCA Gly CAA GTT Gln	CTC Glu 550 CAG GTC Gln 70 GGA CCT	GAA CTT Glu OO GTT	GCT CGA Ala GGA CCT Gly AAT	CAA GTT Gln 660 GCT CGA Ala	TGA Thr CAA GTT Gln 710 CCT GGA	GCT CGA Ala CAG GTC Gln	CAG GTC GIn CCA GGT Pro	CGA Ala> 70 GCA CGT Ala> 720 GTT	
GGTTCAA	AAT TTA Asn CAA GTT Gln GCA CGT	CTT GAA Leu GAG CTC Glu CCT GGA	AAG Phe 40 GGT CCA Gly 690 TCT AGA Ser	AGA Ser GTT CAA Val CAA GTT Gln	GGT CCA Gly CAA GTT Gln	CTC Glu 550 CAG GTC Gln 70 GGA CCT	GAA CTT Glu 00 GTT CAA Val	GCT CGA Ala * GGA CCT Gly * AAT TTA Asn	CAA GTT Gln 660 GCT CGA Ala	CAA GTT Gln 710 CCT GGA	GCT CGA Ala CAG GTC Gln	CAG GTC GIn CCA GGT Pro	CGA Ala> TO GCA CGT Ala> TZE GTT CAA	
GGTTCAA	AAT TTA Asn CAA GTT Gln	CTT GAA Leu GAG CTC Glu CCT GGA	AAG Phe 40 GGT CCA Gly 690 TCT AGA Ser	AGA Ser GTT CAA Val	GGT CCA Gly CAA GTT Gln	CTC Glu 550 CAG GTC Gln 70 GGA CCT	GAA CTT Glu OO GTT	GCT CGA Ala * GGA CCT Gly * AAT TTA Asn	CAA GTT Gln 660 GCT CGA Ala	CAA GTT Gln 710 CCT GGA	GCT CGA Ala CAG GTC Gln	CAG GTC GIn CCA GGT Pro	CGA Ala> TO GCA CGT Ala> TZE GTT CAA	
CGT Ala CAA CAA CAA CAA A TGI A Thr	AAT TTA Asn CAA GTT Gln GCA CGT Ala	GAG CTC Glu  CCT GGA Pro	AAG Phe 40 GGT CCA Gly 690 TCT AGA Ser	AGA Ser GTT CAA Val CAA GTT Gln 740	GGT CCA Gly CAA GTT Gln GGC CCG Gly	CTC Glu 550 CAG GTC Gln 70 GGA CCT Gly	GAA CTT Glu 00 GTT CAA Val	GCT CGA Ala GGA CCT Gly AAT TTA Asn	CAA GTT Gln 6600 GCT CGA Ala TCT AGA Ser	TGA Thr CAA GTT Gln 710 CCT GGA Pro	GCT CGA Ala CAG GTC Gln CAA Val	CAG GTC GIn 6 CCA GGT Pro	CGA Ala> GCA CGT Ala> TZE GTT CAA Val>	
CGT Ala CAA CAA CAA CAA CAA CAA CAA CAA CAA CA	AAT TTA Asn CAA GTT Gln CGCA CGT Ala GTT CAA	GAG CTC GGA Pro	AAG Phe  40 GGT CCA Gly 690 TCT AGA Ser	AGA Ser GTT CAA Val CAA GTT Gln AAT TAA	GGT CCA Gly CAA GTT Gln GGC CCG Gly	CTC Glu 550 CAG GTC Gln 70 GGA CCT Gly	GAA CTT Glu 00 GTT CAA Val	GCT CGA Ala GGA CCT Gly AAT TTA Asn	CAA GTT Gln 6600 GCT CGA Ala TCT AGA Ser	TGA Thr CAA GTT Gln 710 CCT GGA Pro	GCT CGA Ala CAG GTC Gln CAA Val	CAG GTC GIn 6 CCA GGT Pro	CGA Ala>  GCA CGT Ala>  TZE GTT CAA Val> GCT CGA	
CGT Ala CAA CAA CAA CAA CAA CAA CAA CAA CAA CA	AAT TTA Asn CAA GTT Gln CGCA CGT Ala GTT CAA	GAG CTC GGA Pro	AAG Phe  40 GGT CCA Gly 690 TCT AGA Ser	AGA Ser GTT CAA Val CAA GTT Gln AAT TAA	GGT CCA Gly CAA GTT Gln GGC CCG Gly	CTC Glu 550 CAG GTC Gln 70 GGA CCT Gly	GAA CTT Glu 00 GTT CAA Val	GCT CGA Ala GGA CCT Gly AAT TTA Asn	CAA GTT Gln 6600 GCT CGA Ala TCT AGA Ser	TGA Thr CAA GTT Gln 710 CCT GGA Pro	GCT CGA Ala CAG GTC Gln CAA Val	CAG GTC GIn 6 CCA GGT Pro	CGA Ala> GCA CGT Ala> TZE GTT CAA Val>	
CGT Ala CAA CAA CAA CAA CAA CAA CAA CAA CAA CA	AAT TTA Asn CAA GTT GIn CCAA CGT Ala CGT CAA CTT CAA CTT CAA	GAG CTC GLU  CCT GGA Pro  GAT CTA ASP	AAG Phe  40 GGT CCA Gly 690 TCT AGA Ser	AGA Ser GTT CAA Val CAA GTT Gln 740 AAT ASE	GGT CCA Gly CAA GTT Gln GGC CCG Gly	CTC Glu 550 CAG GTC Gln 70 GGA CCT Gly	GAA CTT Glu 00 GTT CAA Val	GCT CGA Ala GGA CCT Gly AAT TTA Asn	CAA GTT Gln 6600 GCT CGA Ala TCT AGA Ser	TGA Thr CAA GTT Gln 710 CCT GGA Pro	GCT CGA Ala CAG GTC Gln CAA Val	CAG GTC GIn 6 CCA GGT Pro AAT TTA Asn	CGA Ala>  GCA CGT Ala>  TZE GTT CAA Val> GCT CGA	
CGT Ala CAA CAA CAA CAA CAA CAA CAA CAA CAA CA	AAT TTA Asn CAA GTT Gln CGCA CGT Ala GTT CAA	GAG CTC GLU  CCT GGA Pro  GAT CTA ASP	AAG Phe  40 GGT CCA Gly 690 TCT AGA Ser	AGA Ser GTT CAA Val CAA GTT Gln 740 AAT ASE	GGT CCA Gly CAA GTT Gln GGC CCG Gly	CTC Glu 550 CAG GTC Gln 70 GGA CCT Gly	GAA CTT Glu 00 GTT CAA Val	GCT CGA Ala GGA CCT Gly AAT TTA Asn	CAA GTT Gln 6600 GCT CGA Ala TCT AGA Ser	TGA Thr CAA GTT Gln 710 CCT GGA Pro	GCT CGA Ala CAG GTC Gln CAA Val	CAG GTC GIn 6 CCA GGT Pro AAT TTA Asn	CGA Ala>  GCA CGT Ala>  TZE GTT CAA Val> GCT CGA	
GGTT CAA CGT ACA A TGT A TGT A TGT A TGT A TGT	CAA GTT GIn GCA CGT Ala CAA GTT CAA GTT TCAA CTT	GAG CTC GGA Pro	AAG Phe  40 CCA Gly 690 TCT AGA Ser CGA	AGA Ser  GTT CAA Val  CAA GTT Gln  740  AAT TTA	GGT CCA Gly CAA GTT Gln GGC CCG Gly ACA TGT Thr	CTC Glu 550 CAG GTC Gln 70 GGA CCT Gly TCA AGT Ser	GAA CTT Glu 00 GTT CAA Val 750 • CTT GAA Lev	GCT CGA Ala GGA CCT Gly AAT TTA Asn CCT CGA Ala	CAA GTT Gln 6600 GCT CGA Ala TCT AGA Ser	TGA Thr CAA GTT Gln 710 CCT GGA Pro 7 A ATI	GCT CGA Ala CAG GTC Gln CAA Val	CAG GTC GIn 6 CCA GGT Pro AAT TTA Asn	CGA Ala>  GCA CGT Ala>  TZE GTT CAA Val> GCT CGA	
CGT Ala CAA CAA CAA CAA CAA CAA CAA CAA CAA CA	CAA GTT Gln GCA CGT Ala CAA GTT Ala CAA GTT CAA GTT CAA GTT TAA GTT TA	GAG CTC GGA Pro	AAG Phe  40 GGT CCA Gly 690 TCT AGA Ser GGT CGA Ala	AGA Ser GTT CAA Val CAA GTT Gln AAT TAA AST CAA GTT GTT CAA GTT GTT CAA GTT CA	GGT CCA Gly CAA GTT Gln GGC CCG Gly ACA TGT Thr	CTC Glu 550 CAG GTC Gln 70 GGA CCT Gly TCA AGT Ser	GAA CTT Glu 00 GTT CAA Val CTI GAA Leu	GCT CGA Ala GGA CCT Gly AAT TTA Asn CCA Ala 800	CAA GTT Gln 6600 GCT CGA Ala TCT AGA Ser Lys	TGA Thr CAA GTT Gln 710 CCT GGA Pro 7 A ATT TAA S Ile	GCT CGA Ala CAG GTC Gln CAA CAA CAA CTT TTC A AAA	CAG GTC GID CCA GGT Pro AAT TTA ASD AAT TTA	CGA Ala>  CGT Ala>  TZI CAA Val>  CGT CGA Ala>	
	ACA TGT Thr 49 AGT Ser	AAC CAA TTG GTT Asn Gln  440 ACA GCT TGT CGA Thr Ala  490 TCA CTT AGT GAA Ser Leu  540 GCA ACC CGT TGG Ala Thr	AAC CAA ATG TTG GTT TAC ASN Gln Met  440 ACA GCT GAA TGT CGA CTT Thr Ala Glu  490 TCA CTT TCA AGT GAA AGT Ser Leu Ser  540 GCA ACC CAA CGT TGG GTT Ala Thr Gln	AAC CAA ATG CAC TTG GTT TAC GTG Asn Gln Met His  440	AAC CAA ATG CAC ATG TTG GTT TAC GTG TAC ASN Gln Met His Met  440	AAC CAA ATG CAC ATG TTA TTG GTT TAC GTG TAC AAT Asn Gln Met His Met Leu  440 450  ACA GCT GAA GAG CTT GGA TGT CGA CTT CTC GAA CCT Thr Ala Glu Glu Leu Gly  490 500  TCA CTT TCA GGG CTT CAA AGT GAA AGT CCC GAA GTT Ser Leu Ser Gly Leu Gln  540 550  GCA ACC CAA GAT GAA GCT CGT TGG GTT CTA CTT CGA Ala Thr Gln Asp Glu Ala	AAC CAA ATG CAC ATG TTA TCA TTG GTT TAC GTG TAC AAT AGT Asn Gln Met His Met Leu Ser  440 450 46  ACA GCT GAA GAG CTT GGA ATG TGT CGA CTT CTC GAA CCT TAC Thr Ala Glu Glu Leu Gly Met  490 500  TCA CTT TCA GGG CTT CAA GCG AGT GAA AGT CCC GAA GTT CGC Ser Leu Ser Gly Leu Gln Ala  540 550  GCA ACC CAA GAT GAA GCT ATT CGT TGG GTT CTA CTT CGA TAA Ala Thr Gln Asp Glu Ala Ile	AAC CAA ATG CAC ATG TTA TCA AAC TTG GTT TAC GTG TAC AAT AGT TTG Asn Gln Met His Met Leu Ser Asn  440 450 460  ACA GCT GAA GAG CTT GGA ATG CAG TGT CGA CTT CTC GAA CCT TAC GTC Thr Ala Glu Glu Leu Gly Met Gln  490 500 510  TCA CTT TCA GGG CTT CAA GCG TCT AGT GAA AGT CCC GAA GTT CGC AGA Ser Leu Ser Gly Leu Gln Ala Ser  540 550  GCA ACC CAA GAT GAA GCT ATT GCT CGT TGG GTT CTA CTT CGA TAA CGA Ala Thr Gln Asp Glu Ala Ile Ala	AAC CAA ATG CAC ATG TTA TCA AAC AAA TTG GTT TAC GTG TAC AAT AGT TTG TTT Asn Gln Met His Met Leu Ser Asn Lys  440  450  460  ACA GCT GAA GAG CTT GGA ATG CAG CCT TGT CGA CTT CTC GAA CCT TAC GTC GGA Thr Ala Glu Glu Leu Gly Met Gln Pro  490  500  510  TCA CTT TCA GGG CTT CAA GCG TCT TGG AGT GAA AGT CCC GAA GTT CGC AGA ACC Ser Leu Ser Gly Leu Gln Ala Ser Trp  540  550  560  GCA ACC CAA GAT GAA GCT ATT GCT GTA CGT TGG GTT CTA CTT CGA TAA CGA CAT Ala Thr Gln Asp Glu Ala Ile Ala Val	AAC CAA ATG CAC ATG TTA TCA AAC AAA TCT TTG GTT TAC GTG TAC AAT AGT TTG TTT AGA ASN Gln Met His Met Leu Ser Asn Lys Ser  440  450  460  460  ACA GCT GAA GAG CTT GGA ATG CAG CCT GCA TGT CGA CTT CTC GAA CCT TAC GTC GGA CGT Thr Ala Glu Glu Leu Gly Met Gln Pro Ala  490  500  510  TCA CTT TCA GGG CTT CAA GCG TCT TGG ACT AGT GAA AGT CCC GAA GTT CGC AGA ACC TGA Ser Leu Ser Gly Leu Gln Ala Ser Trp Thr  540  550  560  GCA ACC CAA GAT GAA GCT ATT GCT GTA AAT CGT TGG GTT CTA CTT CGA TAA CGA CAT TTA Ala Thr Gln Asp Glu Ala Ile Ala Val Asn	AAC CAA ATG CAC ATG TTA TCA AAC AAA TCT GCT TTG GTT TAC GTG TAC AAT AGT TTG TTT AGA CGA ASN Gln Met His Met Leu Ser Asn Lys Ser Ala  440 450 460 470  ACA GCT GAA GAG CTT GGA ATG CAG CCT GCA AAA TGT CGA CTT CTC GAA CCT TAC GTC GGA CGT TTT Thr Ala Glu Glu Leu Gly Met Gln Pro Ala Lys  490 500 510 50  TCA CTT TCA GGG CTT CAA GCG TCT TGG ACT TTA AGT GAA AGT CCC GAA GTT CGC AGA ACC TGA AAT Ser Leu Ser Gly Leu Gln Ala Ser Trp Thr Leu  540 550 560  GCA ACC CAA GAT GAA GCT ATT GCT GTA AAT ATT CGT TGG GTT CTA CTT CGA TAA CGA CAT TTA TAA Ala Thr Gln Asp Glu Ala Ile Ala Val Asn Ile	AAC CAA ATG CAC ATG TTA TCA AAC AAA TCT GCT TCT TTG GTT TAC GTG TAC AAT AGT TTG TTT AGA CGA AGA ASN Gln Met His Met Leu Ser Asn Lys Ser Ala Ser  440 450 460 470  ACA GCT GAA GAG CTT GGA ATG CAG CCT GCA AAA ATT TGT CGA CTT CTC GAA CCT TAC GTC GGA CGT TTT TAA Thr Ala Glu Glu Leu Gly Met Gln Pro Ala Lys Ile  490 500 510 520  TCA CTT TCA GGG CTT CAA GCG TCT TGG ACT TTA AGA AGT GAA AGT CCC GAA GTT CGC AGA ACC TGA AAT TCT Ser Leu Ser Gly Leu Gln Ala Ser Trp Thr Leu Arg  540 550 560 570  GCA ACC CAA GAT GAA GCT ATT GCT GTA AAT ATT TAT CGT TGG GTT CTA CTT CGA TAA CGA CAT TTA TAA ATA Ala Thr Gln Asp Glu Ala Ile Ala Val Asn Ile Tyr	AAC CAA ATG CAC ATG TTA TCA AAC AAA TCT GCT TCT CAA TTG GTT TAC GTG TAC AAT AGT TTG TTT AGA CGA AGA GTT ASN Gln Met His Met Leu Ser ASN Lys Ser Ala Ser Gln  440 450 460 470  ACA GCT GAA GAG CTT GGA ATG CAG CCT GCA AAA ATT AAC TGT CGA CTT CTC GAA CCT TAC GTC GGA CGT TTT TAA TTG Thr Ala Glu Glu Leu Gly Met Gln Pro Ala Lys Ile ASN  490 500 510 520  TCA CTT TCA GGG CTT CAA GCG TCT TGG ACT TTA AGA GTT AGT GAA AGT CCC GAA GTT CGC AGA ACC TGA AAT TCT CAA Ser Leu Ser Gly Leu Gln Ala Ser Trp Thr Leu Arg Val  540 550 560 570  GCA ACC CAA GAT GAA GCT ATT GCT GTA AAT ATT TAT GCA CGT TGG GTT CTA CTT CGA TAA CGA CAT TTA TAA ATA CGT Ala Thr Gln Asp Glu Ala Ile Ala Val Asn Ile Tyr Ala	AAC CAA ATG CAC ATG TTA TCA AAC AAA TCT GCT TCT CAA AAT TTG GTT TAC GTG TAC AAT AGT TTG TTT AGA CGA AGA GTT TTA ASN Gln Met His Met Leu Ser Asn Lys Ser Ala Ser Gln Asn>  440

830 840 850 860 820 AGA CTT GAA TCT ATA AAG AAT AGT ACT GAG TAT GCA ATT GAA AAT CTA TCT GAA CTT AGA TAT TTC TTA TCA TGA CTC ATA CGT TAA CTT TTA GAT Arg Leu Glu Ser Ile Lys Asn Ser Thr Glu Tyr Ala Ile Glu Asn Leu> 870 880 890 900 AAA GCA TCT TAT GCT CAA ATA AAA GAT GCT ACA ATG ACA GAT GAG GTT TTT CGT AGA ATA CGA GTT TAT TTT CTA CGA TGT TAC TGT CTA CTC CAA Lys Ala Ser Tyr Ala Gln Ile Lys Asp Ala Thr Met Thr Asp Glu Val> 940 920 930 960 GTA GCA GCA ACA ACT AAT ATG ATT TTA ACA CAA TCT GCA ATG GCA ATG CAT CGT CGT TGT TGA TTA TAC TAA AAT TGT GTT AGA CGT TAC CGT TAC Val Ala Ala Thr Thr Asn Met Ile Leu Thr Gln Ser Ala Met Ala Met> 990 980 970 1000 ATT GCG CAG GCT AAT CAA GTT CCC CAA TAT GTT TTG TCA TTG CTT AGA TAA CGC GTC CGA TTA GTT CAA GGG GTT ATA CAA AAC AGT AAC GAA TCT Ile Ala Gln Ala Asn Gln Val Pro Gln Tyr Val Leu Ser Leu Leu Arg> 1010 TAA ATT \*\*\*>

FIGURE 40 (3 of 3)

### Alignment List

Search Analy Search from Date: Octobe Time: 15:03:	1 to er 22	101	1 wh	ence ere	: B3 orig	1-41 in =	kD 1		Scor	ix: e Re imum	gion	fro	m 1	to 1	011	
Database: U	serFo	lder	: 41	kD	Flag	elli	n c]	ones	5							
)		*	1	0	*		20		*	30 *	•	*	4	0	*	
B31-41kD	ATG TAC	TAA AAT	ATC	AAT	CAT	TAA	ACA	TCA	GCT	TTA	AAT	GCT	TCA	AGA	AAT	AAT TTA
1. KA-41ki [ 3996 ]	D 		1	0		•••	20	•••		30 		•••		0	•••	>
2. P-Gau-	4	• • •	1	0		•••	20			30		•••		0	•••	>
3. BO-41k [ 3684 ]										30						>
4. DK29-4 [ 3672 ]	1			.0			20			30	• • •	•••		0	•••	>
5. PKO-41 [ 3672 ]															• • •,	>
	50		_	60				70	_		80		_	90		
B31-41kD		TTA	AAC TTG	GCT	GCT	AAT	CTT	AGT	AAA	ACT	CAA	GAA	AAG	CTT	TCT	AGT TCA
1. KA-41k [ 3996 ]									•		80		• • •	90	•••	>
2. P-Gau- [ 3696 ]	450 .c.		t	60				70		с	80	g		90		>
3. BO-41k [ 3684 ]										с		g				>
4. DK29-4	150 t	•••	t	60	•••		•••	70 	• • •		80		•••			>
5. PKO-41			t	60		•••	•••	70 		c	80	g	•••	90 .c.		>
	1	00			110		.*	120	)	*	1	30			140	
B31-41kD										GAT A CTA					GGA	

	•		-20	* 40
1. KA-41kD 100 [ 3996 ]g	110	120		>
2. P-Gau-4 100 [ 3696 ]t	110	120	130	140 tg>
3. BO-41kD 100 [ 3684 ]t	110	120	130	140
4. DX29-41 100 [ 3672 ]t	110 a	120	130	140 tg>
5. PKO-41k 100 [ 3672 ]	110	120	130	140
150	160	170	180	190
413.5 · mom com 330	איייי אאיי כרד	CAA ATA AGA	GGT TTG TCA	CAA GCT TCT AGA GTT CGA AGA TCT
1 2006 1				190>
2. P-Gau-4 150 [ 3696 ]c	160	170 c.	180 ca	190
3. BO-41kD 150	160	170	180 ca	190
4. DK29-41 150 [ 3672 ]g	160	170	180	190>
5. PKO-41k 150 [ 3672 ]c	160	170	180 ca	190
200	. 21	0 :	220	230 240
B31-41kD AAT ACT TC TTA TGA AG	A AND GOT AT	TA TTT TAA T	T CAG ACA ACA	GAA GGG AAT TTA
1. KA-41kD 200 [ 3996 ]	21		220 • • • • • • • • • • • • • • • • • • •	230 240>
2. P-Gau-4 200 [ 3696 ]c	21	.c	220	230 240 a
3. BO-41kD 200 [ 3684 ]c	) 21	.c	220	230 240 a
4. DK29-41 200 [ 3672 ]c	) 2:	10	220	230 240
5. PKO-41k 200 [ 3672 ]c	2	10	220	230 240

				25	: n		_				270			26	20		
		•	*		*	•	4	*		*	*		*	28	*		
<b>B</b> 3	1-41kD	AAT TTA	GAA CTT	CAT CAT	CAA CTT	AAA TTT	GTC CAG	ATT AAT	CAT CAT	AGA TCT	TAC	TTC	CTT	AAC	GCA CGT	CAA	CAA GTT
`	1. KA-41kI	)		25	50		2	260			270			28			
I	3996 ]	•••	•••	•••	•••	•••	• • •	• • •	• • •	•••	•••	• • •	•••	• • •	•••	•••	>
ſ	2. P-Gau-4 3696 ]	1 		25	50		t	260	•••	•••	270 	a		28 a	30	•••	>
ſ	3. BO-41ki 3684 ]	<b>.</b>		25	50		t	260			270	a		.28	30		>
-																	
ſ	4. DK29-4: 3672 ]	•••	•••		•••	•••	t		•••	•••		ā	·	a	•••	•••	>
r	5. PKO-411 3672 ]	k		25	50		t	260			270	a		28 a	30		>
٠	JU12 ,	•••	•••	•••	•••	•••	• • • •			•••			- • •	•••		•••	
	:	290			300			3	10	•	:	320		•	330		*
B3	11-41kD	TCA AGT	GGT	AAC	GGC	ACA	TAT	TCA	GAT	GCA	GAC	AGA	GGT		ATA	CAA	ATT TAA
ſ	1. KA-41ki 3996 ]	290			300			3:	10		:	320			330		>
•	2. P-Gau-									•						•••	
I	3696 ]			•••	a	g		٠	c	• • •	•••	•••		•••	330	g	>
	3. BO-41k	290			300			3	10		:	320					
	3684 ]													•••	•••	g	>
	4. DK29-4: 3672 ]																
-																	
	5. PKO-413																
		_										_					
			40			350								•			
·B	31-41kD	GAA CTT	ATA TAT	GAG CTC	CAA	CTT GAA	ACA TGT	GAC	GAA	TTA AAT	TAA ATT	AGA TCT	ATT TAA	GCT CGA	GAT CTA	CAA GTT	GCT CGA
	1. KA-41k 3996 ]												70			380	>
	2. P-Gau-					350						3	70			380	
ſ	3696 ]													• • •			>
	3. BO-41k 3684 }													•••			>
	4. DK29-4	1 3	40			350			360	)		3				380	

	•								•								
I	3672 ]	•••	•••	• • •	•••	•••	• • •	• • •	• • •	•••	•••	•••	• • •	•••	• • •	•••	>
I	5. PKO-41k 3672 ]			•••		50	•••		360	•••	•••	37	0	•••		g	>
	31-41kD															43 CAA	
В.	31-41KD	GTT	ATA	TTG	GIT	TAC	GTG	TAC	AAT	AGT	TTG	TTT	AGA	CGA	AGA	GTT	TTA
ı	1. KA-41kI 3996,]	•••	390	•••	•••	40	00	•••		110	•••	·	420 	•••	•••	43	>
I	2. P-Gau-4 3696 ]	•••	• • •	• • •	•••	•••	• • •	• • •	∙•g	•••	•••		··· · ·	• • •	с	• • •	>
-	3. BO-41ki 3684 }	• • •		• • •	•••	• • •	•••	• • •	g	•••	•••	•••	• • •	•••	с	• • •	>
I	4. DK29-41 3672 ]	•••	• • •	• • •	• • •	• • •	•••	• • •	g	•••	•••	• • •	• • •	• • •	с	• • •	>
Į	5. PKO-411 3672 ]	k 	390	• • •	···	40	00	•••	g	410	•••		420	•••	с	43	>
		*															
B	31-41kD	GTA CAT	AGA TCT	ACA TGT	GCT CGA	GAA CTT	GAG CTC	CTT GAA	GGA CCT	DTA TAC	CAG GTC	CCT GGA	GCA CGT	AAA TTT	TTA AAT	AAC TTG	ACA TGT
	1. KA-41ki 3996 ]			440	•••		450 				60 	•••	•••	470 			
1	2. P-Gau-															•••	
I	3. BO-41k 3684 ]			440	•••	•••	450 	•••			60 	•••	•••	470 •••	• • •	• • •	
	4. DK29-4 3672 ]			440	•••	• • •	450 a				60 a		•••	470 		•••	
ſ	5. PKO-41 3672 ]		.a.	440	•••		450		•••		60	•••	•••	470 	•••	•••,	480 >
			•	4	90			500		•	510			5	20		
B	31-41kD															GTT CAA	
į	1. KA-41k 3996 }				90				•••	· ••	510				20		>
I	2. P-Gau- 3696 ]				90		a	500 tc.		t	510				20		>

ſ	3. BO-41kI 3684 ]			90	•••	a	00 tc.	• • •	t	510		•••		0	•••	>
ſ	4. DK29-41	L	q	90	•••	a	00 tc.		t	510		•••	52			>
-	5. PKO-41	ς	- 4	90		5	00			510			52	20		
Ι	3672 ]	•••	• •••	•••	•••	a	tc.	• • •		•••	•••	•••	•••	•••	• • •	• • • •
	· , .	530	*	540		•	55	50 *	•	5	60		•	570		*
B	31-41kD	GTT GG CAA CC								CGA		TTA				
I	1. KA-41ks	530	• • •	540 .a.			55	50		5	60			570		>
	2. P-Gau-	530		540			5:	50		5	60			570		
I	3696 ]	g	• • • •	.at	•••	• • •	• • •	a	•••	•••	•••	•••	•••	• • •	t	>
ſ	3. BO-41k9							50 a						570 	t	>
	4. DK29-45 3672 ]															>
	5. PKO-419													570		
	3012 ]	g		.at				a							t	>
٠	3072 ]															>
	3672 ]															>
	31-41kD	580	T GC	A AAT	590 CTT	TTC	* TCT	600 * GGT	GAG	• GGA	61 GCT	IO • CAA	ACT	GCT	520 CAG	GCT
В	31-41kD	580 * AAT GT TTA CA	T GC.	TAA A	590 CTT GAA 590	TTC AAG	* TCT AGA	600 # GGT CCA	GAG CTC	GGA CCT	61 GCT CGA	CAA GTT	ACT TGA	GCT CGA	CAG GTC	GCT CGA
B	31-41kD 1. KA-41k	580 * AAT G1 TTA CA D 580	T GC.	A AAT TAA A	590 CTT GAA 590	TTC AAG	* TCT AGA	600 * GGT CCA 600	GAG CTC	GGA CCT	61 GCT CGA 61	CAA GTT 10	ACT TGA	GCT CGA	CAG GTC 520	GCT CGA
B	31-41kD  1. KA-41k 3996 ]  2. P-Gau- 3696 ]  3. BO-41k	580 * AAT GT TTA CA D 580 4 580	T GC.	A AAT AATT AATT AATT AATT AATT AATT AA	590 CTT GAA 590 	TTC AAG 	* TCT AGA	600 GGT CCA 600 	GAG CTC	GGA CCT	61 GCT CGA 61 	CAA GTT 10	ACT TGA	GCT CGA	CAG GTC 520 	GCT CGA >
Bi I	1. KA-41k 3996 ] 2. P-Gau- 3696 ] 3. BO-41k 3684 ]	580 * AAT GT TTA CF D 580 	T GC.	ATA A	590 CTT GAA 590  590	TTC AAG 	* TCT AGA g	600 * GGT CCA 600  600	GAG CTC	GGA CCT	61 GCT CGA 61 	CAA GTT 10 	ACT TGA	GCT CGA	CAG GTC 520  520 	GCT CGA
Bi I	31-41kD  1. KA-41k 3996 ]  2. P-Gau- 3696 ]  3. BO-41k 3684 ]  4. DK29-4 3672 ]	580 AAT GI TTA C2 D 580 4 580 D 580	T GC.	ATA A	590 CTT GAA 590  590 	TTC AAG  t	* TCT AGA g	600 GGT CCA 600  600 	GAG CTC	GGA CCT	61 GCT CGA 61 	CAA GTT 10 	ACT TGA  g	GCT CGA	CAG GTC 520  520 	GCT CGA >
Bi I I I I	1. KA-41k 3996 ] 2. P-Gau- 3696 ] 3. BO-41k 3684 ]	580 AAT GI TTA C2 D 580 4 580 D 580	T GC.	ATA A	590 CTT GAA 590  590	TTC AAG	TCT AGA	600 CCA 600  600  600	GAG CTC	GGA CCT	61 GCT CGA 61  63	10 CAA GTT 10 	ACT TGA	GCT CGA	520 CAG GTC 520  520 	GCT CGA
Bi I I I I	1. KA-41k 3996 ] 2. P-Gau- 3696 ] 3. BO-41k 3684 ] 4. DK29-4 3672 ]	580 AAT GI TTA CA D 580 	T GC.	ATA A	590 CTT GAA 590  590  590	TTC AAG	TCT AGA	600 CCA 600  600  600 	GAG CTC	GGA CCT	61 GCT CGA 61  63	10 CAA GTT 10 	ACT TGA	GCT CGA	620 CAG GTC 520  520  620	GCT CGA > >

1. KA-41kD [ 3996 ]	630	640	650	660	670
2. P-Gau-4 [ 3696 ]	630 t	640 c.	650 g.a	660 g a	
3. BO-41kD [ 3684 ]	630 t	640 c.	650 g.a	660 g a	670 a>
4. DK29-41 [ 3672 ]	630	640 ac.	650 a	660 • • • • • • • • • • • • • • • • • • •	670
	630 t	640 c.	650 g.a	660 ·ga	670 1 a>
*	680 *	690	700	710	720
B31-41kD CCT GGA	GCT ACA GCA CGA TGT CGT	CCT TCT CAA GGA AGA GTT	GGC GGA GTT AAT CCG CCT CAA TTA	T TCT CCT GTT	AAT GTT
1. KA-41kD [ 3996 ]	680	690	700	710	720 >
2. P-Gau-4 [ 3696 ]	680	690 a	700	710	720 >
3. BO-41kD [ 3684 ]	680	690 a	700	710	720 >
4. DK29-41 [ 3672 ]	680 g	690 g	700	710	720 >
5. PKO-41k [ 3672 ]		690 a	700	710	720 >
	730	740	750	760	·
B31-41kD ACA	ACT ACA GTT	GAT GCT AAT		AAA ATT GAA	AAT GCT
1. KA-41kD [ 3996 ]	730	740	750	760	
	730 c	740	750	760 a	
3. BO-41kD [ 3684 ]		740	•	760 a	·>
4. DK29-41 [ 3672 ]	730	740	750	760 a	>
5. PKO-41k [ 3672 }	730	740	750	760	

					•	روم	32		•					
	770	•	780		<b>.</b> 7	90	•	. 8	00	٠	•	810		•
B31-41kD	ATT A	OTA ADA	ATA I	AGT G. ICA C	AT CAA TA GTT	AGG	GCA CGT	TAA:	ATT AAT	CCA	GCT CGA	TTC AAG	CAA	TTA ATT
1. KA-41)	c770		780		7	90		8	00			810		
[ 3996 ]	•••	• • • • • • • • • • • • • • • • • • • •	•••	•••	•• •••	• • •	•••	•••	•••	• • •	• • •	•••	• • •	>
2. P-Gau-	-770		780			'90 a			00	•••	•••	810	•••	>
3. BO-41)												810		
3. BO-41) [ 3684 ]		• • • • • • • • • • • • • • • • • • • •			••••	a	•••	•••	•••	•••	• • •	•••	•••	>
4. DK29-	4770		780			790		8	00 ~			810		
[ 3672 ]	•••	•••	• • • •	••••	••••	a	• • •	• • •	•••	•••	•••	• • •	• • •	>
5. PKO-4	1770		780		•	790		8	00			810		_
[ 3672 ]	•••	• • • • •	•	•••	•••	a	•••	•••	•••	•••	•••	•••	• • •	>
	82	0 .	. 8	30	*	840		•	85	50	*	8	360	
B31-41kD	AGA	CTT GAI	A TCT	ATA A	AAG AA'	r AGT	ACT	GAG	TAT	GCA	ATT	GAA	AAT	CTA
														GN1
1. KA-41 [ 3996 ]	kd 82 	0		30		840	• • •	. <b></b>		50			360	>
2. P-Gau	_4 82	0	\$	รรก		840	١		89	50		1	360	
[ 3696 ]		•••	`	•••			• • • •	•••	•••	t	•••	•••	•••	>
3. BO-41 [ 3684 ]	kD 82	0	8	330		. 840	)		8	50		1	360	
[ 3684 ]	•••	•••	• • • • •	• • •	• • • • •		:	•••	•••	t	•••	• • •	• • •	>
4. DK29- [ 3672 ]	41 82	20	ς σ	830		840	)		8	50		1	860 C	>
5. PKO-4	1k 82	20 ••••••		B30 •••	••• ••	0	) :			50 t		• • •	B60 •••	>
		870		88	0		890			900	)		9	10
B31-41kD	AAA TTT	CGT AC	TAT TE	CGA	CAA AT	TA AA	A GAT	r GCT A CGA	ACA TGT	ATC CAT,	TG1	CTA	CTC	CAA
1. KA-43	lkD			88					•	900			_	10
[ 3996 ]	• • •	•••	• • • •	• • •	•••	• • •			•••	• • •	•••	• • • •	• • •	>
2. P-Gav [ 3696 ]				88	30		890			900				910
• -														
3. BO-4: [ 3684 ]	lkD 			88			890				) 		-	910 >
4. DK29				88	30 .		890			90	D		9	910
[ 3672 ]	• • •	•••	• • • • •	• • • •	• • • •	• • • •	• ••	• • • •	• • • •	• • •	• • •	• • • •	• •	

	5. PKO-41)	ς .	870			88	30		8	390						91	
I	3672 ]	•••	•••	•••	•••	•••	•••	•••	• • •	•••	• • •	•••	•••	•••	•••	•••	>
		_	9	920			930			94	10	•	•	950			960
B	31-41kD		GCA	GCA	ACA	ACT	AAT	ATG	ATT	TTA	ACA	CAA	TCT	GCA		GCA	ATG
	1. KA-41ki 3996 ]																
	2. P-Gau-4											• '		950			960
I	3696 ]															•••	
I	3. BO-41kI 3684 }							.gt							• • •		960
	4. DK29-4: 3672 ]															•••	960 >
	5. PKO-41)																
i	3672 ]	•••	•••	t	•••	•••	a	.gt	•••	•••	t	•••	• • •	•••	•••	•••	>
			•	9	70	•		980			990		•	10	00	_	
B.	31-41kD	ATT TAA	GCG CGC	CAG	GCT	AAT	CAA	GTT	CCC	CAA	TAT	GTT	TTG	TCA		CTT	AGA TCT
Ī	1. KA-41ki 3996 }													100	00		_
	2. P-Gau-															•••	••••
I	3696 ]	••••	a	•••	•••		• • •	•••	t	• • •	•••			• • • •	• • • •		>
,	3. BO-41ki 3684 ]										990			100	00		
	·															•••	>
I	4. DK29-43 3672 ]	•••		a	•••			980	t	• • •	990	• • •		100			<b>&gt;</b>
ſ	5. PKO-411													10	00		
	30.2 ,	•••		•••	•••	•••	•••	•••	•••	•••	•••	•••	•••	• • •	• • •	•••	•••>
	10	010															
В	31-41kD	TAA ATT															
I	2. P-Gaul	010	>														

Sequence Ran	ge: 1 to 82	2	•				
	_	10	20	30	•	40	
OspA-B31	ATG AAA AAA TAC TTT TTI	TAT TAT ATA	TTG GGA AT VAC CCT TA	'A GGT CTA AT CCA GAT	ATA TTA ( TAA TAT	GCC TTA ATA GC CGG AAT TAT CG	A T
OspA-B31 [ 3288 ]		10	20 	30		40	.>
Ospa-Ka [ 3288 ]	;	10	20 	30	•••	40	• <b>-&gt;</b> ,
Ospa-N40 [ 3276 ]		10	20 	30		40	.>
OspA-ZS7 [ 3264 ]	••• •••	10		30	•••	40	.>
OspA-25015 [ 2802 ]	•••	10	20	30	•••	40 t	.>
OSDA-TRO [ 2648 ]	•••		20			40	.>
OspA-K48 [ 2584 ]	••• •••		20			40	>
OspA-HE 11 [ 2580 ]			20		•••	40	>
OspA-DK29 [ 2566 ]			20		•••	40	>
OspA-1p90 [ 2562 ]			20	30  30	•••	a	>
OspA-BO [ 2558 ]	•••	10.	20	30	•••	40	.:>
OSPA-1P3 [ 2558 ]	•••		20 	30	•••	40	>
OspA-PKO [ 2558 ]	••• •••	10	20	30	•••	40	>
OSPA-ACAI [ 2556 ]		10	20		•••	40	>
ospa-P-GAU [ 2544 ]	••• •••	10					>
	50	60 *	<b>7</b> (	• •	80	90	•
OspA-B31	TGT AAG CA	AA AAT GTT IT TTA CAA	AGC AGC (	CTT GAC GAG GAA CTG CTY	DAA AAA E DTT TTT C	AGC GTT TCA G	ATA CAT

FIGURE 42 (1 of 16)

///	//33
,,,,	,,,,

OspA-B31	50	60	70	80	90
[.3288] OspA-KA	50	60	70	80	90
[ 3288 ]		•••			>
OspA-N40 [ 3276 ]	50	60	70 	80	90>
OspA-ZS7 [ 3264 ]	50	60	70 	80	90 >
OspA-25015 [ 2802 ]	50	60	70	80	90>
OspA-TRO [ 2648 ]	50	60	70 t	80	90>
OspA-K48 [ 2584 ].	50	60	70 ·	80 at	90>
OspA-HE 11 [ 2580 ]	50	60	70 t	80 at	90 >
OspA-DK29 [ 2566 ]	50	60	70 t	80 at	90 >
OspA-Ip90 [ 2562 ]	50	60	t	80 at	90 >
OspA-BO [ 2558 ]	50 c	60	70 t	80 a	90 .c>
OSPA-IP3 [ 2558 ]	50 c	60	70 t	80 . a	90 .c>
OspA-PKO [ 2558 ]	50 c	60	70	80 a	90 .c>
OspA-ACAI [ 2556 ]	50 c	60	70	80 a	90 .c>
ospa-P-GAU [ 2544 ]	50c	60	t	80 a	90 .c>
	100	110	120	130	140
OspA-B31	GAT TTG CCT CTA AAC GGA	GGT GAA AT	G AAA GTT CTT C TTT CAA GAA	GTA AGC AAA GAA CAT TCG TTT CTT	AAA AAC AAA TIT TIT TIT
OspA-B31 [ 3288 ]	100	110	120	130	140>
OspA-KA [ 3288 ]	100	110	120	130	>
Ospa-N40	100	110	120	130	140

FIGURE 42 (2 of 16)

SUBSTITUTE SHEET (RULE 26)

		•			
[ 3276 ]			.c	•••	>
OspA-ZS7 [ 3264 ]	100	110	.c	130	140>
OspA-25015 [ 2802 ]	100		120		140 g>
OspA-TRO [ 2648 ]	100 a		120	130	140 g>
OspA-X48 [ 2584 ]	100 a	110 g	120 c	t	140 g>
OspA-HE 11 [ 2580 ]	100 a	110 g	120	<del>-1</del> 30 t	140 g>
OspA-DK29 [ 2566 ]	100 a	110 g	120 c	130 t	140>
OspA-Ip90 [ 2562 ]	100 a	110 g c	120	130 t	140 g>
OspA-BO [ 2558 ]	100	110 g	120		
OSPA-IP3 [ 2558 ]	100	110 gt .	120	130 t	140 g>
OspA-PKO [ 2558 ]	100	110 g	120	130 t	140 g>
Ospa-ACAI [ 2556 ]	100	110 g	120 '		140 g>
ospa-P-GAU [ 2544 ]	. 100	110g	120	130 t	140 g>
	150	160	170	180	190
OspA-B31	GAC GGC AAG CTG CCG TTC	TAC GAT CTA A	ATT GCA ACA GTA FAA CGT TGT CAT	GAC AAG CTT CTG TTC GAA	GAG CTT AAA CTC GAA TTT
OspA-B31 [ 3288 ]	150	160	170	180	190
Ospa-Ka [ 3288 ]	150	160	170	180	190 >
OspA-N40 [ 3276 ]	150	160	170	180	190
OspA-ZS7 [ 3264 ]	150	160	170	180	>
OspA-25015 [ 2802 ]	150	160 ag	170	180	190

FIGURE 42 (3 of 16)

# SUBSTITUTE SHEET (RULE 26)

OspA-TRO [ 2648 ]	150 tt	a	160 ag	g		• •••		180	a	•••		90 >
OspA-K48 [ 2584 ]	150 t	a	160 ag	gag			•••	180	•••	•••		90
OspA-HE 11 [ 2580 ]	150 tt	a	160 ag	g	170		a	180	,	•••		90 •••>
OspA-DK29 [ 2566 ]	150 t	a	160 ag	gag	170	• •••	· · ·	180	•••	•••		90
OspA-Ip90 [ 2562 ]	150 tt	a	160 ag	g			•••	180	• • •			90 •••>.
OspA-BO [ 2558 ]	150		160 ag	.ag	170	• •••	•••	180		•••		90
OSPA-IP3 [ 2558 ]	150		160 ag	.ag			•••	180		•••	19 a	
OspA-PKO · · [ 2558 ]	150 t		160 ag	.ag	170	• •••	• • •	180	a	•••	19 a	
Ospa-ACAI [ 2556 ]	150 t		160 ag	.ag	170		•••	180	a		19 a	
ospA-P-GAU [ 2544 ]	150 t		160 ag	.ag	170			180	a	•••	a	
·	2	00	210			220	•	2	30			240
OspA-B31	GGA ACT C	TCT GAT AGA CTA	AAA AAC	AAT	GGA TO	T GGA	GTA	CTT	GAA	GGC	GTA CAT	AAA TTT
OspA-B31 [ 3288 ]	2	00	210			220	•••		30	•••		240 >
OspA-KA [ 3288 ]		00	210									240 >
OspA-N40 [ 3276 ]		00	210		•••				230			240 >
OspA-ZS7 [ 3264 ]		00				220			230	•••		240
OspA-25015 [ 2802 ]	a	200	210		•••	220 • • • • g	•.•g		230		•••	240 >
OspA-TRO [ 2648 ]		200	210 g.		t .	220	ac.		230	t	.a.	240 >
OspA-K48 [ 2584 ]	2	200	210			220	ac.		230	t	.a.	240

FIGURE 42 (4 of 16)

Ospa-HE 11	200 210 220 230 240
[ 2580 ]	200 210 ac
OspA-DK29 [ 2566 ]	200 210 220 act .a>
OspA-Ip90 [ 2562 ]	200 210 220 230 240 ac
OspA-BO [ 2558 ]	200 210 220 230 240
OSPA-IP3 [ 2558 ]	200 210 220 230 240 g
OspA-PKO [ 2558 ]	200 210 220 230 240
Ospa-ACAI [ 2556 ]	200 210 220 230 240 g
ospa-P-GAU	200 210 220 230 240 gt ac>
1 2211 1	250 260 270 280
OspA-B31	GCT GAC AAA AGT AAA GTA AAA TTA ACA ATT TCT GAC GAT CTA GGT CAA CGA CTG TTT TCA TTT CAT TTT AAT TGT TAA AGA CTG CTA GAT CCA GTT
OspA-B31 [ 3288 ]	250 260 270 280
OspA-KA [ 3288 ]	250 260 270 280
Ospa-N40 [ 3276 ]	250 260 270 280
OspA-ZS7 [ 3264 ]	250 260 270 280
OspA-25015 [· 2802 ]	250 260 270 280 c g g a.c ac.>
OspA-TRO [ 2648 ]	250 260 270 280 t
OspA-K48 [ 2584 ]	250 260 270 280 a gtc a>
OspA-HE 11 [ 2580 ]	250 260 270 280 a g g g a a >
OspA-DK29 [ 2566 ]	250 260 270 280 a gt.ca>
OspA-Ip90	250 260 270 280

FIGURE 42 (5 of 16)

/	,	5		/3	3
•	•	٧,	′′	_	_

[ 2562 ]	a	•••	• • •	•••	•••	.c.	•••	•••	•••	•••	g	g	•••	•••	a.,	a>
OspA-BO [ 2558 ]	.a.	·•••	25	50	•••		260			270		• • •			•••	a>
OSPA-IP3 [ 2558 ]	.a.			50	•••		260		•••	270 				BO •••	a	a>
OspA-PKO [ 2558 ]	.a.			50	•••		260	•••		270 		• • •		B0 •••	• • •	a>
Ospa-ACAI [ 2556 ]	.a.	•••		50			260		•••		g.,			BO	a	a'>
ospa-P-GAU [ 2544 ]	.a.		2:	50	•••		260	•••	•••	270.		• • •		30	a	a>
	290		•	300		•	3:	10	•		320		*	330		
OspA-B31	ACC TGG	ACA TGT	CTT GAA	GAA	GTT	TTC	AAA	GAA	GAT	GGC	AAA	ACA	CTA	GTA CAT	TCA AGT	AAA TTT
OspA-B31 [ 3288 ]	290			300		• • •	3:	10			320			330		>.
Ospa-Ka [ 3288 ]	290			300				10			320		• • •	330	•••	>
OspA-N40 [ 3276 ]	290			300				10			320		···	330	•••	>
OspA-ZS7 [ 3264 ]	290			300				10			320	•••	• • •	330		>
OspA-25015 [ 2802 ]	290			300		a					320		t	330 g		>
Ospa-TRO [ 2648 ]	290		t	300	a	•••					320		t	330		>
OspA-K48 [ 2584 ]	290 t		t	300				10			320		t	330	• • •	>
OspA-HE 11 [ 2580 ]			t	300		•••					320		t	330	g	>
OspA-DK29 [ 2566 ]		.a.	t	300			_	10			320		t	330	• • •	>
OspA-Ip90 [ 2562 ]	290		t	300	a.c						320	• • •	t	330		>
OspA-BO [ 2558 ]	290	•••	t.c	300				10			320	•••	t	330 ••g		.g.>
OSPA-IP3 [ 2558 ]	290		t.c	300				10			320		t	330 g		.g.>

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OspA-PKO [ 2558 ]	290 t.c	300 c	310	320	330 tgg.>
Ospa-ACAI [ 2556 ]	290	300 c	310	320	330 tgg.>
ospA-P-GAU [ 2544 ]	290 t.c	300 c	. 310	320	330 tgg.>
	340	350	360	· 370	380
OspA-B31	AAA GTA ACT TTT CAT TGA	TCC AAA GAG AGG TTT CTG	C AAG TCA TO G TTC AGT AC	CA ACA GAA GAA ST TGT CTT-CTT	AAA TIC AAT GAA TIT AAG TIA CTI
OspA-B31 [ 3288 ]	340	350	360 	370	380>
OspA-KA [ 3288 ]	340	350	360	370	380>
OspA-N40 [ 3276 ]	340	350	360	370	380>
OspA-ZS7 [ 3264 ]	340	350	360	370	380
OspA-25015	340 ag	350 t	360 t	370	380 >
OspA-TRO [ 2648 ]	340 a	350 t	360 t	370 t	380 c .c.>
OspA-K48 [ 2584 ]	340	350 c ctt	360	370	380>
OspA-HE 1: [ 2580 ]	1 340	350 c ctt	360	370	380 c>
Ospa-DK29 [ 2566 ]	340	350 c ctt	360	370	380 c .g.>
OspA-Ip90 [ 2562 ]	340	350 c ctt	360	370	380 c .c.>
OspA-BO [ 2558 ]	3409	350	360 a a	370 t	380>
OSPA-IP3 [ 2558 ]	340 9	350	360 a a	370 t	380 .tg>
OspA-PKO [ 2558 ]	3409	350	360 a a	370 t	380
Ospa-ACAI [ 2556 ]	340	350	360 a a	370 t	380 . tg>

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ospA-P-GAU [ 2544 ]	340	.gt	50 .g	a	360 a		370 .t	.tg		880
	390	•	400	•	410	•	420		•	430
OspA-B31	AAA GGT TTT CCA	GAA GTA ' CTT CAT	TCT GAA AGA CTT	AAA TTT	TAT TAT	ACA A	CT CGT	CTG	CCT	ACC AGA TGG TCT
OspA-B31 [ 3288 ]	390				•••		•• •••		•••	430>
Ospa-KĀ [ 3288 ]	390	•••	400	•••	410	••••	420		•••	430>
OspA-N40 [ 3276 ]	390			•••	•••	••••			• • •	430>
OspA-ZS7 [ 3264 ]	390				410			•••	•••	430>
OspA-25015 [ 2802 ]	390 c	t	400 gt		410 g	g	420		•••	430 t.>
OspA-TRO [ 2648 ]	390	t	400	• • •	410 .c	ct	420	a	•••	430 g>
OspA-K48 [ 2584 ]	390	ac.	400		410 .c	gt	420	a.t		430 >
OspA-HE 11 [ 2580 ]	390 g	a	400		.c. 410	gt	420 	a.t	•••	430>
OspA-DK29 [ 2566 ]	390	ac.	400		.c	gt		a.t	•••	430>
OspA-Ip90 [ 2562 ]	390	c.	400	• • •	.c	gt	420		•••	430>
OspA-BO [ 2558 ]	390	t.g	400 c.		410 .ccg		420 a.	a.t	•••	430 a.>
OSPA-IP3 [ 2558 ]	390		400 c.		410 .ccg			a.t	•••	430 a.>
OspA-PKO [ 2558 ]	390	t.g	400 c.	•••	410 .ccg		420 a.		•••	430 a.>
Ospa-ACAI [ 2556 ]	390		400 c.		410 .ccg		420 a.		•••	`430 a.>
ospA-P-GAU [ 2544 ]	390	t.g	400 c.		410 .ccg				•••	430 ,a.>
		440	450		4	60		470		480
OspA-B31	CTT GAA	TAC ACA	GGA ATT	AAA	AGC GAT	GGA 1	CT GGA	AAA	GCT	AAA GAG

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	GAA CTT ATG TGT CCT TAA TTT TCG CTA CCT AGA CCT TTT CGA TTT (	CIC
OspA-B31 [ 3288 ]	440 450 460 470	480 >
OspA-KA [ 3288 ]	440 450 460 470	480 >
OspA-N40 [ 3276 ]	440 450 460 470a	480 •••>
OspA-ZS7 [ 3264 ]	440 450 460 470	480 •••>
OspA-25015 [ 2802 ]	440 450 460 470	480 a>
Ospa-TRO [ 2648 ]	440 450 460 470 4	480 a>
OspA-K48 [ 2584 ]	440 450 460 470 4	480 a>
OspA-HE 11 [ 2580 ]	440 450 460 470 4	480 a>
OspA-DK29 [ 2566 ] ·	440 450 460 470 4	480 a>
OspA-Ip90 [ 2562 ]	440 450 460 470 4	480 a>
OspA-BO [ 2558 ]	440 450 460 470 4	480 a>
OSPA-IP3 [ 2558 ]	440 450 460 470 4 t ag a.c	480 ده
OspA-PKO [ 2558 ]	440 , 450 460 470 4 t ag a.c	480 a>
Ospa-ACAI [ 2556 ]	110	480 a>
ospA-P-GAU [ 2544 ]	***	480 a>
	490 500 510 520	
OspA-B31	GTT TTA AAA GGC TAT GTT CTT GAA GGA ACT CTA ACT GCT GAA AAA CAA AAT TTT CCG ATA CAA GAA CTT CCT TGA GAT TGA CGA CTT TTT	ACA TGT
OspA-B31 [ 3288 ]	490 500 510 520	>
OspA-KA [ 3288 ]	490 500 510 520	>

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OspA-N40 [ 3276 ]	•••	490	500	• • • • • • • • • • • • • • • • • • • •	510	520
OspA-ZS7 [ 3264 ]		490 a	500		510 t	520
OspA-25015 [ 2802 ]	ac	490 aa .	500		510	520 g>
OspA-TRO [ 2648 ]	.c:.	490a	500 tc		510 g	520 cc>
		•				cgg
OspA-K48 [ 2584 ]	•••	490	500 t. ac		510 g	5201 530>
						cgg
OspA-HE 11 [ 2580 ]	• • • • • • • • • • • • • • • • • • • •	490	500 t. ac		510 g	5201 530 c>
_	•					cgg
OspA-DK29 [ 2566 ]	•••	490 a	500 t. ac		510 g	5201 530 c>
				•		cgg
OspA-Ip90		490	500	)	510	1 5201 530
[ 2562 ]		a				c>
OspA-BO [ 2558 ]		490 aa	500 t. ac		510 .aa g g	520 aat gt.>
OSPA-IP3 [ 2558 ]		490 aa	500 t. ac		510 .aa g g	520 aat gt.>
OspA-PKO [ 2558 ]		490 aa	50 t. ac		510 .aa g g	520 aat gt.>
OSDA-ACAI						
[ 2556 ]	• • • • • •	490 aa	50 .t.ac		510 .aa g g	520 aat gt.>
ospA-P-GAU [ 2544 ]		aa 490	t. ac 50	 D	.aa g g 510	
ospa-P-GAU		aa 490 aag .	t. ac 50	) )	.aa g g 510 .aa g g	aat gt.> 520 aat gt.>
ospa-P-GAU	530	aa 490	t. ac 50	 D	.aa g g 510	aat gt.>
ospa-P-GAU	ACA TTG	aa 490 aag . 540	t. ac 50 .t. ac	550 GA ACT GTT	.aa g g 510 .aa g g 560 .ACT TTA AGC	aat gt.> 520 aat gt.>
ospa-P-GAU [ 2544 ]	ACA TTG	aa 490 aag . 540	t. ac 50 .t. ac	550 GA ACT GTT	.aa g g 510 .aa g g 560 .ACT TTA AGC	520 aat gt.>  570 * AAA AAT ATT TCA
ospA-P-GAU [ 2544 ] OspA-B31	ACA TTG TGT AAC	490 aag . 540 CAC CAA 1	t. ac 50 .t. ac	550 GA ACT GIT	.aa g g 510 .aa g g 560 .ACT TTA AGC	aat gt.>  520 aat gt.>  570 * AAA AAT ATT TCA TIT TTA TAA AGT

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[ 3288 ]	•••	•••	• • • • • • • • • • • • • • • • • • • •	••• ••• •••	>
OspA-N40 [ 3276 ]	530	• • • •	550	560	570 ··· ··· ··· ···>
OspA-ZS7 [ 3264 ]	530	540	550		570 >
OspA-25015 [ 2802 ]	530	540	550	560 t	570 g c.c>
OspA-TRO [ 2648 ]	530	540 aaac.	550 c	560 gt	570 c.c c>
OspA-K48 [ 2584 ]		540 aaac.	550 c	560- gt	570gct.>
OspA-HE 11 [ 2580 ]		540 aaac.	550 gc	560	570gc>
OspA-DK29 [ 2566 ]		540 aaac.	550 c	560 gt	570gct.>
OspA-Ip90 [ 2562 ]	a	540 aaac.	550 c	560 gt	570 c.c>
OspA-BO [ 2558 ]	530	540 .aaa	550 c	560t	570 g g.a g>
OSPA-IP3 [ 2558 ]	530	540 .aaa	550 c	560 t	570 g g.a g>
OspA-PKO [ 2558 ]	530	540 .aaa	550 c	560 t	570 g g.a g>
Ospa-ACAI [ 2556 ]		540 .aaa		560 t	570 g g.a g>
ospA-P-GAU [ 2544 ]	530	540 .aaa		560 t	570 g g.a g>
	580	590	600	610	620
OspA-B31	AAA TCT TTT AGA	GGG GAA GTT CCC CTT CAA	TCA GTT GAA	CTT AAT GAC ACT GAA TTA CTG TGA	GAC AGT AGT GCT
OspA-B31 [ 3288 ]	580	590			620
OspA-KA [ 3288 ]	580	590	600	610	620
OspA-N40 [ 3276 ]	580	590	600	610	620
OspA-ZS7 [ 3264 ]	580	590	600	610	620 >

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OspA-25015 [ 2802 ]	580 a	590 a ac	60Ó 6	
OspA-TRO [ 2648 ]	580 ca	590 a.a a		10 620 tatcc.cag>
OspA-K48 5 [ 2584 ]		590 60 a.a a		620 tcc. cag>
OspA-HE 115 [ 2580 ]		590 · 60 a.a a		620 tcg>
OspA-DK29 5 [ 2566 ]		90 60 a.a ac		620 tcc.cgg>
OspA-Ip90 5 [ 2562 ]		690 60 a.a a		620 tcc. cag>
OspA-BO [ 2558 ]	580 a	590 a a		10 620 acc. cag>
OSPA-IP3 [ 2558 ]	580a	590 a a		10 620 acc. cag>
Ospa-PKO [ 2558 ]	580a	590 a a		10 620 acc. cag>
OspA-ACAI [ 2556 ]	580 a	590 a a		10 620 acc. cag>
ospa-P-GAU [ 2544 ]	580 a	590 a a		10 620 acc. cag>
	630	640	* * *	660 670
OspA-B31	GCT ACT AAA CGA TGA TTT	AAA ACT GCA GC TTT TGA CGT CG	T TGG AAT TCA GGC A ACC TTA AGT CCG	ACT TCA ACT TTA ACA TGA AGT TGA AAT TGT
OspA-B31 [ 3288 ]	630	640	650	660 670
OspA-KA [ 3288 ]	630	640	650	660 670
OspA-N40 [ 3276 ]	630	640	650	660 670
OspA-ZS7 [ 3264 ]	630	640	650	660 670
OspA-25015 [ 2802 ]	630	640 gg aa	650 a g g	660 670
OspA-TRO [ 2648 ]	630	640 g. aa	650 a g aat	660 670c >

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OspA-K48 [ 2584 ]	630		650 aaa g		670 c>
OspA-HE 11 [ 2580 ]	630 a	640 t.c .g.	650 a.a g		670 t>
OspA-DX29 [ 2566 ]	630	640 	650 aaa g	660 . aag	670 c>
OspA-Ip90 [ 2562 ]	630	640	650 a.a g	660 . aag	670 =>
OspA-BO [ 2558 ]	630	640 gc	650 a g		670
OSPA-IP3 [ 2558 ]	630	640 gc	650 a g	660 . aaat	670
OspA-PKO [ 2558 ]	630	640 gc	650 a g	660 . aaat	670
Ospa-ACAI [ 2556 ]	630	640 gc	650 a g	660 . aaat	670
ospA-P-GAU [ 2544 ]	630	640 gc	650 a g	660 . aaat	670
	680	690	700	710	720
OspA-B31	ATT ACT GTA TAA TGA CAT	AAC AGT AAA TIG TCA TTT	AAA ACT AAA GAG TTT TGA TTT CTG	CTT GTG TTT GAA CAC AAA	ACA AAA GAA TGT TTT CTT
OspA-B31 [ 3288 ]	680	690	700	710	720
OspA-KA [ 3288 ]	680	690	700	710	720
OspA-N40 [ 3276 ]	680	690	700	710	720 >
OspA-2S7 [ 3264 ]	680	690	700	710	720
OspA-25015 [ 2802 ]	680	690 ac	700c.	710 a	720 c>
OspA-TRO [ 2648 ]	680 gg	tc	700 a	710 aa	720
OspA-K48 [ 2584 ]	680 gg	690 tc c	700 c a.,	710 ac	720 >
OspA-HE 11 [ 2580 ]	680 g. aa.	690 a c	700	710 ac	720
OspA-DK29	680	690	700	710	720

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r 2566 1	ggtc cc aac
	710 720
OspA-Ip90 [ 2562 ]	680 690 700 710 720ggtc cgc aac>
OspA-BO [ 2558 ]	680 690 700 710 720gtc
OSPA-IP3 [ 2558 ]	680 690 700 710 720gtc. c.a t c>
OspA-PKO [ 2558 ]	680 690 700 710 720gtc
OspA-ACAI [ 2556 ]	680 690 700 710 720gtc
ospA-P-GAU [ 2544 ]	680 690 700 710 720gtc
	730 740 750 760
OspA-B31	AAC ACA ATT ACA GTA CAA CAA TAC GAC TCA AAT GGC ACC AAA TTA GAG TTG TGT TAA TGT CAT GTT GTT ATG CTG AGT TTA CCG TGG TTT AAT CTC
OspA-B31 [ 3288 ]	730 740 750 760
OspA-KA [ 3288 ]	730 740 750 760
OspA-N40 [ 3276 ]	730 740 750 760
OspA-ZS7 [ 3264 ]	730 740 750 760
OspA-25015 [ 2802 ]	730 740 750 760 g tc a gcaacga>
OspA-TRO [ 2648 ]	730 740 750 760 g a
OspA-K48 [ 2584 ]	730 740 750 760 770 gaagcatca>
OspA-HE 11 [ 2580 ]	730 740 750 760 gaa.cgcatca>
OspA-DK29 [ 2566 ]	730 740 750 760 770 g ag
OspA-Ip90 [ 2562 ]	730 740 750 760 770 g a
OspA-BO [ 2558 ]	730 740 750 760 gatac.gcatta>

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	760	
OSPA-IP3 [ 2558 ·]		ta>
OspA-PKO [ 2558 ]	730 740 750 760 gata	ta>
OspA-ACAI [ 2556 ]	730 740 750 760 gata	ta>
ospa-P-GAU [ 2544,]	730 740 750 760 tata	ta>
• ·	770 780 790 800 81	• •
OspA-B31	GGG TCA GCA GTT GAA ATT ACA AAA CTT GAT GAA ATT AAA AI CCC AGT CGT CAA CTT TAA TGT TTT GAA CTA CTT TAA TTT T	IC GCT TTA IG CGA AAT
OspA-B31 [ 3288 ]		10
OspA-KA [ 3288 ]		10>
Ospa-N40 [ 3276 ]		10>
OspA-ZS7 [ 3264 ]		10
OspA-25015 [ 2802 ]	700 900 8	10
OspA-TRO [ 2648 ]		10
OspA-K48 [ 2584 ]	780 790 800 810c aacc a.a c	
OspA-HE 11	700 900 8	10
OspA-DK29 [ 2566 ]	780 790 800 810c aacc a.a c	
OspA-Ip90 [ 2562 ]	780 790 800 810c aacccg a.a cc	j.t>
OspA-BO [ 2558 ]	770 780 790 800 8	310 >
OSPA-IP3 [ 2558 ]	770 780 790 800 8	310 >
OspA-PKO [ 2558 ]	770 780 790 800 5	810 >

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OSPA-ACAI 770 780 790 800 810 [ 2556 ]c a ac	
820 * Ospa-B31 AAA TAA TTT ATT	
OspA-B31 820 [ 3288 ]>	
OspA-KA 820 [ 3288 ]>	
OspA-N40 820 [ 3276 ]>	
OspA-ZS7 820 [ 3264 ]>	
OspA-25015 [ 2802 ] .g.>	
OspA-TRO 820 [ 2648 ]>	
OspA-K48 820 [ 2584 ]>	
OspA-HE 11 820 [ 2580 ]>	
OspA-DK29 820 [ 2566 ]>	
OspA-Ip90 820 [ 2562 ]>	
OspA-BO 820 ( 2558 )>	
OSPA-IP3 820 [ 2558 ]>	
OspA-PKO 820 [ 2558 ]>	
Ospa-ACAI 820 [ 2556 ]>	
OSPA-P-GAU 820 [ 2544 ]>	

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ATG AAA AAA TAC TTT TTT	TAT TTA	20 TTG GGA	ATA GGT	30 CTA ATA	TTA GC	40  * TTA ATA
50 GCA TGT AAG	60 CAA AAT	gtt age	70 * AGC CTT	* GAT GAA	08 44 A4A	90 * * T AGC GTT
CGT ACA TTC  1  TCA GTA GAT	00	110	•	120 _	~ <b>.</b>	130
AGT CAT CTA	AAT GGA	CCA CCT	160	CAA GAA	CAT TO 170	180 ± ±
AAA GAC AAA TIT CIG TIT	GAC GGT CTG CCA	AAA TAC TTT ATG 200	AGT CTA TCA GAT	GAG GCA CTC CGT	ACA GT TGT CA	T CTG TTC
CTT GAG CTT GAA CTC GAA	AAA GGA	ACT TCT	GAT AAA CTA TIT	AAC AAC	GGT TO	220 * * T GGA ACA IA CCT TGT
230 CTT GAA GGT		ACT GAC		AAA GTA		
*	80	290	•	300	•	310
GCT GAT GAC CGA CTA CTG	CTA AGT GAT TCA	CAA ACT GTT TGA	TTT AAA	GAA ATT	TTC AAG TI	A GAA GAT
320	330		340		350	
320 GCC AAA ACA COG TIT TGT	TTA GTA	TCA AAA	340 4 AAA GTA	ACC CTT	AAA GA	360 AC AAG TCA
GCC AAA ACA COG TTT TGT 3 TCA ACA GAA	TTA GTA ART CAT	TCA AAA AGT TTT 380	340 AAA GTA TTT CAT	ACC CTT TGG GAA 390 GGT GAA	AAA GA	360 AC AAG TCA NG TTC AGT 400 CT GAA AAA
GCC AAA ACA COG TIT TGT  3 TCA ACA GAA AGT TGT CTT	TTA GTA AAT CAT  70  GAA AAA CTT TTT	TCA AAA AGT TTT 380 TTC AAC AAG TTG	340 AAA GTA TTT CAT GAA AAG CTT TTC 430	ACC CTT TGG GAA 390 GGT GAA CCA CTT	AAA GA TOT AC	360 AC AAG TCA TG TTC AGT  400 AC GAA AAA AC CIT TITI  450
GCC AAA ACA CGG TTT TGT  3 TCA ACA GAA AGT TGT CTT  410 ACA ATA GTA TGT TAT CAT	TTA GTA AAT CAT  TO GAA AAA CTT TTT  420	TCA AAA AGT TTT 380 TTC AAC AAG TTG	340 AAA GTA TTT CAT GAA AAG CTT TTC 430 ACC AGA	ACC CTT TGG GAA 390 GGT GAA CCA CTT	AAA GA TOTT CT	360 AC AAG TCA TG TTC AGT  400 AT GAA AAA AA CIT TTT  450 AA GAC ATA
CCC AAA ACA CCG TTT TGT  3 TCA ACA GAA AGT TGT CTT  410 ACA ATA GTA TGT TAT CAT  4 AAA AGC GAT TTT TCG CTA	TTA GTA AAT CAT  70  GAA AAA CTT TTI  420  AGA GCA TCT CGT	TCA AAA AGT TTT  380 TTC AAC AAG TTG AAT GGA TTA CCT 470 CGGA AAA CCT TTT	340 AAA GTA TTT CAT GAA AAG CTT TTC 430 ACC AGA TGG TCT	ACC CTT TGG GAA 390 GGT GAA CCA CTT 4 CTT GAA GAA CTT 480	AAA GA TTT CT ACA TC TGT AC 440 TAC AC TTA AC	360 AC AAG TCA TG TTC AGT  400 AT GAA AAA EA CIT TIT  450 AC GAC ATA ET CTG TAT  490 AA GAC TIT IT CTG AAA
GCC AAA ACA COG TIT TGT  3 TCA ACA GAA AGT TGT CTT  410 ACA ATA GTA TGT TAT CAT	TTA GTA AAT CAT  TO GAA AAA CTT TTI  420 AGA GCA TCT CGT  60 CCT AGG  510 GGA ACC	TCA AAA AGT TTT  380 ATTC AAC AAG TTG AAG TTG ATTA CCT  470 CGA AAA CCT TTT	340 AAA GTA TTT CAT GAA AAG CTT TTC 430 ACC AGA TGG TCT 520 CGA TTT	ACC CTT TGG GAA 390 GGT GAA CCA CTT 480 GAA CTT 480 CGA GTT CAA	AAA GA TTT CI ACA TC TGT AC TAC TAC AC TAC TAC AC TAC TAC AC TAC TAC AC TAC TAC TAC AC TAC TAC TAC TAC TAC	360 AC AAG TCA NG TTC AGT  400 AT GAA AAA GA CIT TITT  450 AA GAC ATA GT CTG TAT  490 AA GAC TITT AAA  CA TTG AAA  CA TTG AAA

K48/Tro Ospa

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Wednesday, April 27, 1994 11:37 AM CAA TGT CTT CCG TGA CAA CAA AAT TCG TTC TTG TAA AAT TTT AGG 630 590 GGA GAA ATA ACA GTT GCA CTT GAT GAC TCT GAC ACT ACT CAG GCT CCT CTT TAT TGT CAA CGT GAA CTA CTG AGA CTG TGA TGA GTC CGA 670 650 660 640 \* \* ŧ ACT ANA ANA ACT OGA ANA TOG GAT TOA ANT ACT TOO ACT TTA ACA TGA TIT TIT TGA CCT TIT ACC CTA AGT TTA TGA AGG TGA AAT TGT 690 700 ATT AGT GTG AAT AGC AAA AAA ACT AAA AAC ATT GTA TIT ACA AAA TAN TON CAC TIN TOG TIT TIT TGN TIT TTG TAN CAT ANN TGT TIT 750 730 GAA GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTT CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA

790

CTA GAA GGC AAC GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA GAT CTT CCG TTG CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT

800

810

820

780

AAC GCT TTA AAA TAG TTG CGA AAT TTT ATC

770

••	· 1	.0	•		20		•	30		•	4	<b>10</b>	•
ATG AAA TAC TTT	AAA TTT	TAT ATA	ATT TAA	TTG AAC	GGA CCT	ATA TAT	GCT CCA	CTA GAT	ATA TAT	ATT AAT	CGG	ATT TAA	ata Tat
50			60		•	•	70	•		80		•	90
GCA TGC CGT ACG	AAG	CAA GTT	AAT TTA	GTT CAA	AGC TCG	AGC TCG	CTT GAA	GAT CTA	GAA CTT	AAA TTT	AAC TTG	AGC TCG	GCT CGA
•		00	•'		110		•	120		= v- •	•	30 *	•
TCA GTA AGT CAT	GAT CTA	TTG AAC	CCT GGA	CCA	CAG CTC	ATC	AAA	CAR	GAA	CAT	AGT	AAA TTT	CAA CTT
140		•	150		•	1	60		:	170			180
AAA GAC	AAA TTT	GAC	CCA	AAG	TAC	AGI	CTA GAI	AAC TIC	CG1	ACA TOT	CAT	GAC	AAG TTC
		90	*		200		*	210	k	•		20	•
ATT GAG	CTA	AAA TTT	GGA	ACT TGA	TC1	GAT	AAA TTT	GAC	C AAT	r GG1 A CC2	TC:	GGA CCT	CAC
230		*	240	t	4		250		•	260		*	270
CTT GA	A GGT	L ACA	AAA TT	GA!	GA(	AA G TT	A AG	AA T TT A	A GC T CG	A AAI T TT	A TT	A ACA I TGI	ATT TAA
•	-	280	,	<b>A</b>	290		•	30	•	•		310	•
GCT GA CGA CT	C GA	T CTA	A AG T TC	r aa a tt	A AC T TG	C AC	TT AA	C C1	A CT T GA	TT TT	A AA T TT	A GAI T CT	A GAT CTA
320	<b>)</b>		33	0	•		340		*	350	)	•	360
GGC AF	A AC	A TT AA T	A GT T CA	G TC	A AG	IA AI	IA G1	A A. VT TA	TE TO	OA TO	A GA	AA OA	A ACA T TGT
	•	370		*	380	r		-	90	•		400	•
TCA AC AGT TO	CA GA	T GA	TA A.	C A	K A	AT G	AA AA T TT	AA G	GT G CA C	AA T	ig ty	CT GC GA CG	AAA A TTT TS
41	0	•	42	20		r	430		*	44		•	450
ACC A	TYC 2/	A AC	BA GI	AA A	лт С	GA A	CC A GG T	AA C	TT G	T AA A TT	A TA T AT	CA GI GT CI	LA ATG
		450			47	0	•	. 4	180		•	490 *	•
A AAA I TIT	CC C	AT G	GA A CT T	GC C	GA A CT I	AA ( TT (	GA 1	AA (	AAE TTC	T TIE	A AT	AA AA TT T	ag tit TC aaa
50	*	•		10		•	520		•	53	•	*	540 *
ACT ( TGA (	TTT G	D AA	GA A	AA C	TA (	GA '	AAT ( TTA (	TAE ATC	AAA TTT	CAT 1	ACA 1 I'GT 1	MTG G AAC C	AA GTA TT CAT
	*	550	١	٠		50 •		ŧ	570			580	*
AAA (	AAS	GA A	voc (	er i	CT.	TTA	agt .	AAG	GAA	TTA	GCA .	RAA 1	nct oga

P-GAU/BO-OSPA Wednesday, April 27, 1994 11:22 AM

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TTT CTT CCT TGG CAA TGA AAT TCA TTC CTT TAA CGT TTT AGA CCT

590 600 610 620 630

GAA GTA ACA GTT GCT CTT AAT GAC ACT AAC ACT ACT CAG GCT ACT
CTT CAT TGT CAA CGA GAA TTA CTG TGA TTG TGA TGA GTC CGA TGA

AGT GTT AAC ACC AAA AAA ACT ACA CAA CTT GTG TTT ACT AAA CAA TCA CAA TTG TCG TTT TTT TGA TGT GTT GAA CAC AAA TGA TTT GTT

GAC ACA ATA ACT GTA CAA AAA TAC GAC TCC GCA GGT ACC AAT TTA

770 780 790 800 810

GAA GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC
CTT CCG TGT CGT CAG CTT TAA TIT TGT GAA CTA CTI GAA TIT TTG

820

GCT TTA AAA TAG CGA AAT TTT ATC

1	10	20		30		40
ATG AAA AAA TAC TIT TIT	ATT TAT TAA ATA	TTG GGA AAC CCT	ATA OCT TAT CCA	CTA I	ATT ATA	CCC TTA ATA
50 ±	60		70	•	80	90
GCA TGT AAG CGT ACA TTC	CAA AAT GIT TTA	GTT AGC CAA TCG	AGC CIT TCG GAA	GAC C	EAG AAA	AAC AGC GTT TTG TCG CAA
. 10	0	110		120		130
TCA GTA GAT AGT CAT CTA	TTG CCT AAC GGA	GGT GAA CCA CTT	ATG AAA TAC TTT	GTT (	CTT GTA	AGC AAA GAA TCG TTT CTT
140	150	•	160	*	170	180
AAA AAC AAA TTT TIG TTT	GAC GGC CTG CCG	AAG TAC TTC ATG	GAT CTA CTA GAT	ATT (	CA ACA	GTA GAC AAG CAT CTG TTC
<b>1</b> 9	0	200	•	210	•	220
CTT GAG CTT GAA CTC GAA	AAA GGA TIT CCI	ACT TCT TGA AGA	GAT AAA CTA TTT	AAC I	AAT GGA	TCT GGA GTA AGA CCT CAT
230	240		250	•	260	270
CTT GAA GGC GAA CTT CCG	GTA AAA CAT TTT	GCT GAC CGA CTG	AAA AGT TTT TCA	AAA (	TA AAA CAT TTT	TTA ACA ATT AAT TGT TAA
28	30	290	•	300	•	310
TCT GAC GAT AGA CTG CTA	CTA GGT GAT CCA	CAA ACC GTT TGG	ACA CTT TGT GAA	GAA (	TTT TTC	AAA GAA GAT TTT CTT CTA
320	330	•	340	•	350	360
GGC AAA ACA CCG TTT TGT	CTA GTA GAT CAT	TCA AAA AGT TTT	AAA GTA- TTT CAT	ACT TGA	TCC AAA AGG TTT	GAC AAG TCA CTG TTC AGT
37	70	380	•	390	•	400
TCA ACA GAA AGT TGT CTT	GAA AAA CTT TTT	TTC AAT AAG TTA	GAA AAA CTT TTT	CCA (	GAA GTA CTT CAT	TCT GAA AAA AGA CTT TTT
410	420	•	430	•	440	450
ATA ATA ACA TAT TAT TGT	AGA GCA TCT CGT	AAT GGA TTA CCT	ACC AAA TGG TIT	CTT GAA	GAA TAT CTT ATA	ACA GAA ATG TGT CTT TAC
<b>4</b> 6	50	470 *	*	480	į	490
AAA AGC GAT TTT TCG CTA	GGA ACC	GGA AAA CCT TTT	GCT AAA CGA TTT	GAA CTT	GTT TTA CAA AAT	AAA AAG TTT TTT TTC AAA
500 *	510	•	520	•	530	540
ACT CTT GAA TGA GAA CTT	GGA AAA CCT TTT	GTA GCT CAT CGA	AAT GAT	AAA	GTA ACA CAT TGT	TTG GAA GTA AAC CTT CAT
51	50	560	•	570		580
	-	•	-	-	•	•

B31-PBK Mednesday, April 27, 1994 11:19 AM

TTT CTT CCT TGG CAA TGA AAT TCA TTC CTT TAA AGT TTT AGA COC

610 • GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT GCT ACT CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA CGA TGA

640 650

AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA ATT TIT TIT TGA CGT CGA ACC TTA AGT TIT TGA AGG TGA AAT TGT TAA

720 710 690 700 AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT

750 740 \* GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA

CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT 800 810

GAA GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC CTT CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG

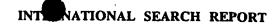
820

780

OCT TTA AAA TAA CGA AAT TTT ATT

30 ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA TAC TIT TIT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT 80 70 60 50 GCA TGC AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA AAC AGC GCT CGT ACG TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTG TCG CGA . 110 TCA GTA GAT TTG CCT GGT GAG ATG AAA GTT CTT GTA AGT AAA GAA AGT CAT CTA AAC GGA CCA CTC TAC TIT CAA GAA CAT TCA TIT CIT 160 \* AAA GAC AAA GAC GGT AAG TAC AGT CTA AAG GCA ACA GTA GAC AAG TIT CTG TIT CTG CCA TIC ATG TCA GAT TIC CGT TGT CAT CTG TIC 200 190 ATT GAG CTA AAA GGA ACT TCT GAT AAA GAC AAT GGT TCT GGA GTG TAA CTC GAT TIT CCT TGA AGA CTA TIT CTG TTA CCA AGA CCT CAC 260 240 \* CTT GAA GGT ACA AAA GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GAA CTT CCA TGT TTT CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA 290 300 GCT GAC GAT CTA AGT AAA ACC ACA TTC GAA CTT TTA AAA GAA GAT CGA CTG CTA GAT TCA TIT TGG TGT AAG CTT GAA AAT TIT CTT CTA 320 330 GGC AAA ACA TTA GTG TCA AGA AAA GTA AGT TCT AGA GAC AAA ACA CCG TIT TGT AAT CAC AGT TCT TIT CAT TCA AGA TCT CTG TIT TGT 390 380 TCA ACA GAT GAA ATG TTC AAT GAA AAA GGT GAA TTG TCT GCA AAA AGT TGT CTA CTT TAC AAG TTA CTT TTT CCA CTT AAC AGA CGT TTT 430 420 ACC ATG ACA AGA GAA AAT GGA ACC AAA CTT GAA TAT ACA GAA ATG TOG TAC TGT TCT CTT TTA CCT TGG TTT GAA CTT ATA TGT CTT TAC 480 AAA AGC GAT GGA ACC GGA AAA GCT AAA GAA GTT TTA AAA AAG TTT TIT TCG CTA CCT TGG CCT TTT CGA TTT CIT CAA AAT TTT TTC AAA 530 510 520 ACT CTT GAA GGA AAA GTA GCT AAT GAT AAA GTA ACA TTG GAA GTA TGA GAA CIT CCT TIT CAT CGA TTA CTA TIT CAT TGT AAC CIT CAT 56C AAA GAA GGA ACC GTT ACT TTA AGT AAG GAA ATT TCA AAA TCT GGG

TIT CIT CCT TGG CAA TGA AAT TCA TTC CIT TAA AGT TIT AGA CCC 600 610 GAA GIT TCA GIT GAA CIT AAT GAC ACT GAC AGT AGT GCT GCT ACT CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA CGA TGA 660 . 640 650 AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA ATT TIT TIT TGA CGT CGA ACC TTA AGT TIT TGA AGG TGA AAT TGT TAA 700 690 \* \* \* AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT 750 740 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA OGC ACC AAT CTA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT 780 790 800 770 GAA GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC CTT CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG OCT TTA AAA TAA CGA AAT TTT ATT



Intern al Application No.
PCT/US 94/12352

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/31 C12N15/62 C07K14/20 A61K39/02 G01N33/50 C07K16/12 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 6 C07K C12N A61K G01N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages 1,6,7,9, X MOLECULAR MICROBIOLOGY, 22,27, vol.6, no.20, 1992 pages 3031 - 3040 28,30,45 ROSA P. A. ET AL. Recombination between genes encoding major outer surface proteins A and B of Borrelia burgdorferi' see the whole document Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the document defining the general state of the art which is not considered to be of particular relevance invention earlier document but published on or after the international document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to filing date document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) involve an inventive step when the document is taken alone document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled document referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report n 3. 03. 95 24 February 1995 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 Espen, J

Form PCT/ISA/210 (second sheet) (July 1992)

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#### INTERNATIONAL SEARCH REPORT

Intern al Application No PCT/US 94/12352

	PC1/US 94/12352
Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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JOURNAL OF BACTERIOLOGY, vol.175, no.9, May 1993 pages 2516 - 2522 KITTEN T. ET AL. 'Intragenic recombination and a chimeric outer membrane protein in the relapsing fever agent Borrelia hermsii' see the whole document	1,6-8, 22,27-29
WO,A,93 08306 (SYMBICOM AKTIEBOLAG) 29 April 1993 see claims 44-46	1-9, 22-30, 45-48
WO,A,91 13630 (THE UNITED STATES OF AMERICA) 19 September 1991 see page 8; figures 11,13	1-9, 22-30, 45-48
WO,A,94 20536 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 15 September 1994 see page 4-6; claim 6	1,6,22, 27
	Modern approaches to new vaccines including prevention of AIDS. Tenth annual meeting, Cold Spring Harbor, New York, USA, September 1992.' 1993, COLD SPRING HARBOR LABORATORY PRESS, NEW YORK cited in the application McGrath B. C. et al.: 'Biochemical and biophysical characterization of the major outer surface protein from north american and european isolates of Borrelia burgdorferi' see page 365 - page 370 see page 369, last paragraph  JOURNAL OF BACTERIOLOGY, vol.175, no.9, May 1993 pages 2516 - 2522 KITTEN T. ET AL. 'Intragenic recombination and a chimeric outer membrane protein in the relapsing fever agent Borrelia hermsii' see the whole document  WO,A,93 08306 (SYMBICOM AKTIEBOLAG) 29 April 1993  see claims 44-46  WO,A,91 13630 (THE UNITED STATES OF AMERICA) 19 September 1991  see page 8; figures 11,13  —————————————————————————————————

#### INTERNATIONAL SEARCH REPORT

Information on patent family members

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